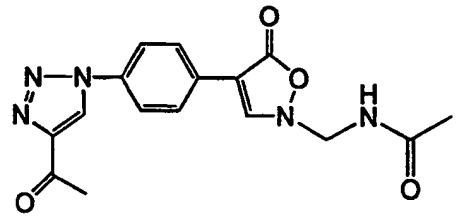
EXAMPLE 18

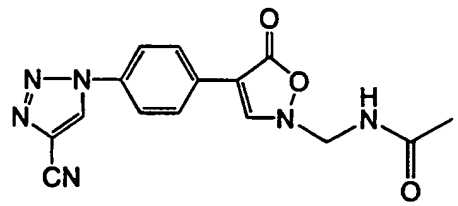
N-({4-[4-(4-acetyl(1,2,3-triazolyl))phenyl]-5-oxo-2-hydroisoxazol-2-yl}methyl)acetamide



A mixture of N-{[4-(4-azidophenyl)-5-oxo-2-hydroisoxazol-2-yl]methyl}acetamide (100 mg, 0.36 mmol) and of 3-butyn-2-one (0.035 mL, 0.72 mmol) in 3 mL DMF was heated at 50°C for 24 hours. The reaction mixture was concentrated in vacuo and then triturated with EtOAc to yield 60 mg (49%) of the title compound as a yellow solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.47 (s, 1 H), 9.35, (s, 1 H), 8.98, (t, J = 6 Hz, 1 H), 8.02 (s, 4 H), 5.08 (d, J = 6 Hz, 2 H), 3.32 (s, 3 H), 1.85 (s, 3 H).

EXAMPLE 19

N-({4-[4-(4-cyano(1,2,3-triazolyl))phenyl]-5-oxo-2-hydroisoxazol-2-yl}methyl)acetamide

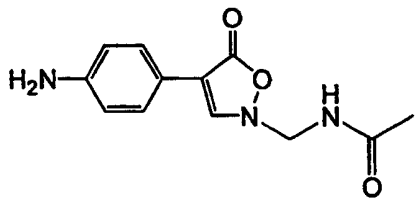


A mixture of N-{[4-(4-azidophenyl)-5-oxo-2-hydroisoxazol-2-yl]methyl}acetamide (500 mg, 1.83 mmol) and 0.8 mL of cyanoacetylene

[prepared according to Murahashi, S.; Takizawa, T.; Kurioka, S.; Maekawa, S.; in J. Chem. Soc. Jap., **77**, p, 1689, 1956] in 5 mL of DMF was heated at 50°C for 48 hours. Upon cooling, the precipitated solid was collected by filtration and washed with DMF to yield 375 mg (63%) of the title compound as a white solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.75 (s, 1 H), 9.17, (s, 1 H), 9.00, (t, *J* = 6 Hz, 1 H), 8.05 (d, *J* = 9 Hz, 2 H), 7.95 (d, *J* = 9 Hz, 2 H), 5.10 (d, *J* = 6 Hz, 2 H), 1.85 (s, 3 H).

EXAMPLE 20

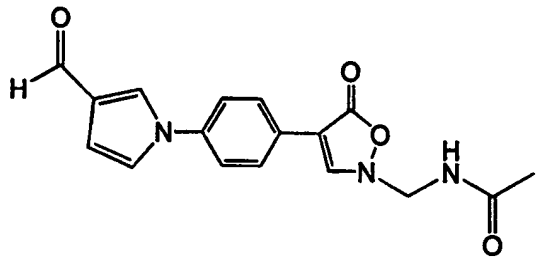
N-{[4-(4-aminophenyl)-5-oxo-2-hydroisoxazol-2-yl]methyl}acetamide



To a mixture of N-{[4-(4-azidophenyl)-5-oxo-2-hydroisoxazol-2-yl]methyl}acetamide (3 g, 10.98 mmol) in 40 mL EtOAc and 20 mL MeOH was added $SnCl_2 \bullet 2H_2O$ (12.5 g, 54.9 mmol). After all of the solid was dissolved, the reaction mixture was concentrated in vacuo and neutralized with saturated aqueous sodium bicarbonate. The mixture was concentrated in vacuo again and the residue was dissolved in a mixture of 4:1 $CHCl_3$/MeOH. The resulting solution was filtered throuth celite, and the insoluble material was discarded. The filtrate was then concentrated in vacuo to yield 3 g (100%) of the title compound as a yellow solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.83, (t, *J* = 6 Hz, 1 H), 8.55, (s, 1 H), 7.43 (d, *J* = 9 Hz, 2 H), 6.56 (d, *J* = 9 Hz, 2 H), 5.21, (broad s, 2 H), 4.91 (d, *J* = 6 Hz, 2 H), 1.82 (s, 3 H).

EXAMPLE 21

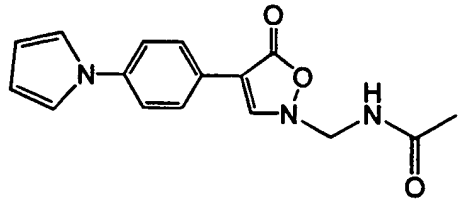
N-({4-[4-(3-formylpyrrolyl)phenyl]-5-oxo-2-hydroisoxazol-2-yl}methyl)acetamide



To a solution of N-{[4-(4-aminophenyl)-5-oxo-2-hydroisoxazol-2-yl]methyl}acetamide (200 mg, 0.81 mmol) in 3 mL of acetic acid was added 2,5-dimethoxy-3-tetrahydrofurancarboaldehyde (184 mg, 1.27 mmol). This mixture was refluxed for 0.5 hours, and then concentrated in vacuo to give the crude product. Purification by silica gel chromatography (eluting with EtOAc, then 8% MeOH in EtOAc) gave 240 mg (91%) of the title compound as a yellow solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.79 (s, 1 H), 9.08, (s, 1 H), 9.00, (t, J = 6 Hz, 1 H), 8.29, (m, 1 H), 7.93 (d, J = 9 Hz, 2 H), 7.74 (d, J = 9 Hz, 2 H), 7.58, (m, 1 H), 6.71 (m, 1 H), 5.06 (d, J = 6 Hz, 2 H), 1.86 (s, 3 H).

EXAMPLE 22

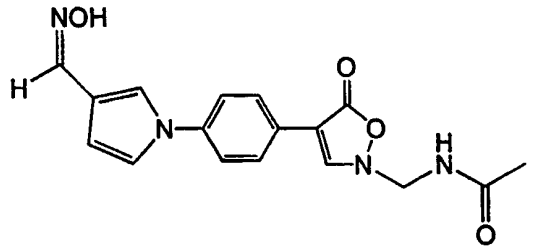
N-{[5-oxo-4-(4-pyrrolylphenyl)-2-hydroisoxazol-2-yl]methyl}acetamide



This compound was prepared from N-{[4-(4-aminophenyl)-5-oxo-2-hydroisoxazol-2-yl]methyl}acetamide as described above for N-({4-[4-(3-formylpyrrolyl)phenyl]-5-oxo-2-hydroisoxazol-2-yl}methyl)acetamide except that 2,5-dimethoxy-3-tetrahydrofuran was used in place of 2,5-dimethoxy-3-tetrahydrofurancarboaldehyde. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.92, (s, 1 H), 8.94, (t, J = 6 Hz, 1 H), 7.85 (d, J = 9 Hz, 2 H), 7.62 (d, J = 9 Hz, 2 H), 7.40, (t, J = 2 Hz, 2 H), 6.27 (t, J = 2 Hz, 2 H), 5.04 (d, J = 6 Hz, 2 H), 1.86 (s, 3 H).

EXAMPLE 23

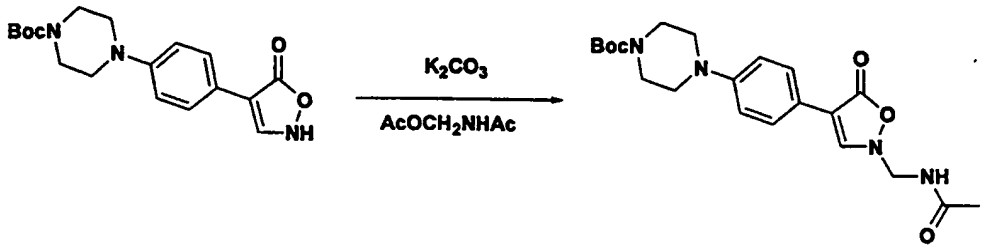
N-[(4-{4-[3-((hydroxyimino)methyl)pyrrolyl]phenyl}-5-oxo-2-hydroisoxazol-2-yl)methyl]acetamide



A mixture of N-({4-[4-(3-formylpyrrolyl)phenyl]-5-oxo-2-hydroisoxazol-2-yl}methyl)acetamide (100 mg, 0.30 mmol) and 50% aqueous NH_2OH (40 mg, 0.60 mmol) in 3 mL of MeOH was heated at reflux for 2 hours. The reaction mixture was then concentrated in vacuo and the residue was triturated with ether to yield 96 mg (94%) of the title compound as a yellow solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.6 (s, 1 H), 9.02, (s, 1 H), 8.95, (t, J = 6 Hz, 1 H), 8.00, (s, 1 H), 7.87 (d, J = 9 Hz, 2 H), 7.66, (s, 1 H), 7.63 (d, J = 9 Hz, 2 H), 7.45, (m, 1 H), 6.50 (m, 1 H), 5.04 (d, J = 6 Hz, 2 H), 1.85 (s, 3 H).

EXAMPLE 24

t-Butyl 4-(4-{2-[(acetylamino)methyl]-5-oxo-2-hydroisoxazol-4-yl}phenyl)piperazine carboxylate



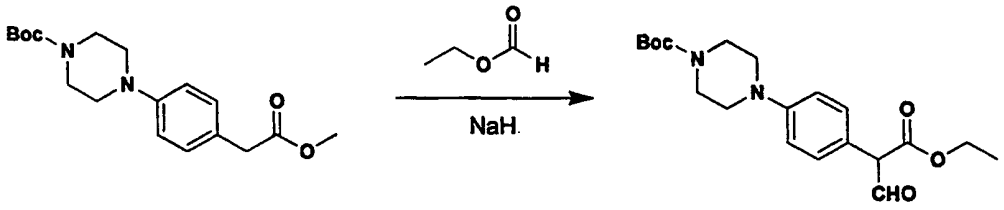
To t-butyl 4-[4-(5-oxo-2-hydroisoxazol-4-yl)phenyl]piperazinecarboxylate (1.5 g, 4.3 mmol) in 35 mL dimethylformamide was added N-(hydroxymethyl)acetamide acetate (2.9 g, 22.0 mmol) followed by potassium carbonate (3.0 g, 22.0 mmol). After 5 hours the reaction mixture was poured into ice water. After 18 hours the precipitate was filtered and dried in vacuo to provide 1.4 g (77%) of the title compound. ^{1}H NMR (methanol-d_4; 300 MHz) δ 8.48 (s, 1H), 7.66 (d, J = 8.8 Hz, 2H), 7.01 (d, J = 8.8 Hz, 2H), 5.07 (s, 2H), 3.58 (t, J = 4.8 Hz, 4H), 3.17 (t, J = 5.2 Hz, 4H), 1.94 (s, 3H), 1.50 (s, 9H); ESI $(M+H)^+$ = 417.

The starting materials were prepared as follows:

Methyl 2-(4-{4-[(t-butyl)oxycarbonyl]piperazinyl}phenyl) acetate

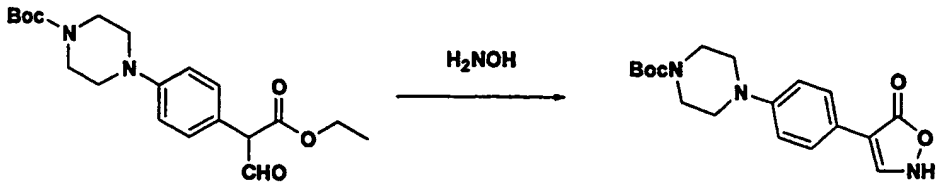
A flask charged with cesium carbonate (4.6 g, 14.0 mmol), palladium (II) acetate (0.07 g, 0.3 mmol), and (S)-BINAP (0.28 g, 4.5mmol) was evacuated and flushed with dry nitrogen. Methyl 2-{4-[(trifluoromethyl)sulfonyloxy]phenyl} acetate (3.0 g, 10.0 mmol) and t-butyl-1-piperazinecarboxylate (2.3 g, 12.0 mmol) in 20 mL toluene was added via syringe and the resultant mixture was stirred at ambient temperature for 30 minutes and at 80°C for 16 hours. The reaction mixture was removed from the heating bath, concentrated, and chromatographed on silica gel (0 to 30% ethyl acetate / hexane) providing 1.7 g (50%) of the title compound. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 3.70 (s, 3H), 3.59 (t, J = 5.0 Hz, 4H), 3.57 (s, 2H), 3.12 (t, J = 5.2 Hz, 4H), 1.50 (s, 9H); ESI $(M+H)^+$ = 335.

Ethyl 2-(4-{4-[(t-butyl)oxycarbonyl]piperazinyl})phenyl)-3-oxopropanoate



To methyl 2-(4-{4-[(t-butyl)oxycarbonyl]piperazinyl}phenyl) acetate (0.67 g, 2.0 mmol) in 8 mL ethyl formate was added sodium hydride (60% dispersion in mineral oil) (0.32 g, 8.0 mmol) portionwise. After 1.5 hours, the reaction mixture was poured into saturated sodium bicarbonate, and extracted three times with ether. The combined organic layers were washed with brine, dried over magnesium sulfate, filtered and concentrated. The crude product was used directly in the next step without further purification.

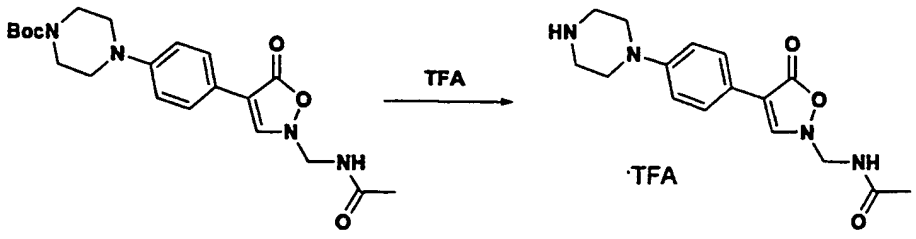
t-Butyl 4-[4-(5-oxo-2-hydroisoxazol-4-yl)phenyl]piperazinecarboxylate



To ethyl 2-(4-{4-[(t-butyl)oxycarbonyl]piperazinyl})phenyl)-3-oxopropanoate (7.8 g, 20.7 mmol) in 140 mL methanol and 40 mL water was added hydroxylamine (50% in water, 3.0 mL, 49.0 mmol). The reaction mixture was heated to reflux for 3 hours, cooled and concentrated. The residue was triturated with water and the precipitate was filtered, dried and washed with ether to provide 4.3 g of the title compound. The aqueous solution was lyophilized providing an additional 1.5 g of the title compound. ^{1}H NMR (methanol-d_4; 300 MHz) δ 8.35 (s, 1H), 7.58 (br d, *J* = , 2H), 6.96 (d, *J* = 8.2 Hz, 2H), 3.58 (t, *J* = 4.6 Hz, 4H), 3.10 (br s, 4H), 1.50 (s, 9H); ESI $(M+H)^+$ = 345.

EXAMPLE 25

N-{[5-oxo-4-(piperazinylphenyl)-2-hydroisoxazol-2-yl]methyl} acetamide trifluoroacetate salt

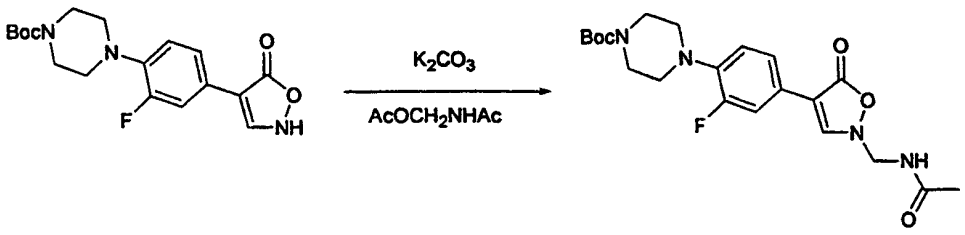


To t-butyl 4-(4-{2-[(acetylamino)methyl]-5-oxo-2-hydroisoxazol-4-yl}phenyl)piperazine carboxylate (0.3 g, 0.7 mmol) in 5 mL dichloromethane was added 2 mL trifluoroacetic acid. After 30 minutes, the reaction mixture was concentrated and triturated with ether to provide

0.3 g (97%) of the title compound. ^{1}H NMR (methanol-d_4; 300 MHz) δ 9.00 (t, J = 6.0 Hz, 1H), 8.23 (s, 1H), 7.70 (d, J = 8.8 Hz, 2H), 7.05 (d, J = 8.7 Hz, 2H), 5.08 (d, J = 6.2 Hz, 2H), 3.45-3.38 (m, 8H), 1.95 (s, 3H); ESI $(M+H)^+$ = 317.

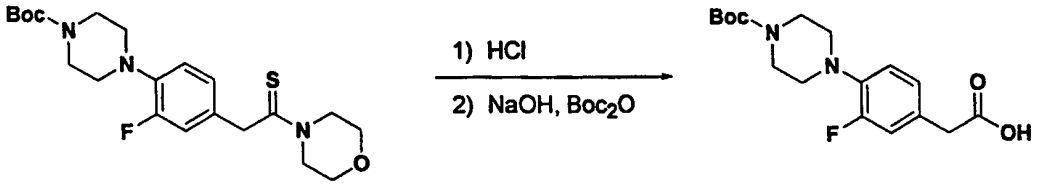
EXAMPLE 26

tert-Butyl 4-(4-{2-[(acetylamino)methyl]-5-oxo(2-hydroisoxazol-4-yl)}-2-fluorophenyl)piperazinecarboxylate



Prepared according to the general procedures outlined in Schemes 1, 3, and 6. The starting materials were prepared as follows:

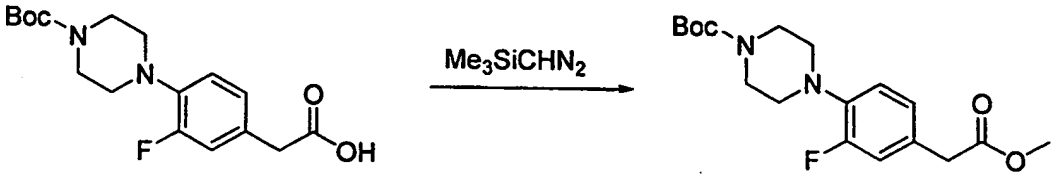
2-(4-{4-[(t-butyl)oxycarbonyl]piperazinyl}-3-fluorophenyl)acetic acid



To t-butyl 4-[2-fluoro-4-(2-morpholin-4-yl-2-thioxoethyl)phenyl]piperazinecarboxylate (4.2 g, 10 mmol) was added 22 mL of concentrated hydrochloric acid at 0°C. The resulting mixture was heated to reflux for 1.5 hours, cooled to 0°C, and 23 mL of 10N sodium hydroxide was added to bring the pH to 14. Then 50 mL water was

added followed by di-t-butyl dicarbonate (5.6 g, 26.0 mmol) in 5 mL tetrahydrofuran. The resulting mixture was allowed to stir at 0°C for 30 minutes and then for 1 hour at ambient temperature at which time it was diluted with 200 mL water. Then 5 mL sodium hydroxide was added to adjust the pH to 14, and the reaction mixture was extracted with ether . The aqueous layer was acidified to pH 3 by the careful addition of 6N hydrochloric acid and then extracted with three portions of ethyl acetate. The organic layer was washed with brine, dried over magnesium sulfate, and concentrated. The resultant residue was dissolved in dichloromethane and hexanes were added to produce a precipitate which was collected by filtration providing 3.0 g (89%) of the title product. ^{1}H NMR ($CDCl_3$; 300 MHz) δ 7.04-6.98 (m, 2H), 6.90 (t, *J* = 8.3 Hz, 1H), 3.60 (m, 6H), 3.02 (t, *J* = 5.0 Hz, 4H), 1.50 (s, 3H); ESI $(M+H)^+$=339.

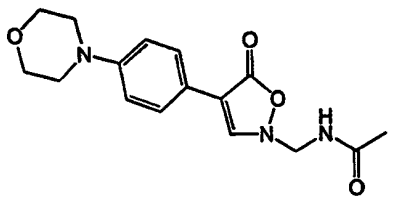
Methyl 2-(4-{4-[(t-butyl)oxycarbonyl]piperazinyl}-3-fluorophenyl)acetate



To 2-(4-{4-[(t-butyl)oxycarbonyl]piperazinyl}-3-fluorophenyl)acetic acid (0.3 g, 1.0 mmol) in 2 mL methanol and 7 mL benzene was added trimethylsilyldiazomethane (0.65 mL, 1.30 mmol). After stirring at ambient temperature for 1 hour, the reaction mixture was concentrated to provide 0.36 g (99%) of the title compound. ^{1}H NMR ($CDCl_3$; 300 MHz) δ 7.00 (m, 2H), 6.90 (t, *J* = 8.3 Hz, 1H), 3.71 (s, 3H), 3.61 (t, *J* = 4.9 Hz, 4H), 3.57 (s, 2H), 3.02 (t, *J* = 5.0 Hz, 4H), 1.50 (s, 9H); ESI $(M+H)^+$ = 353.

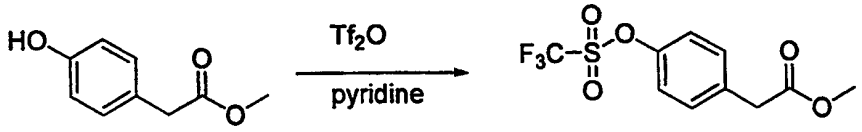
EXAMPLE 27

N-{[4-(4-morpholinylphenyl)-5-oxo-2-isoxazolinyl]methyl}acetamide



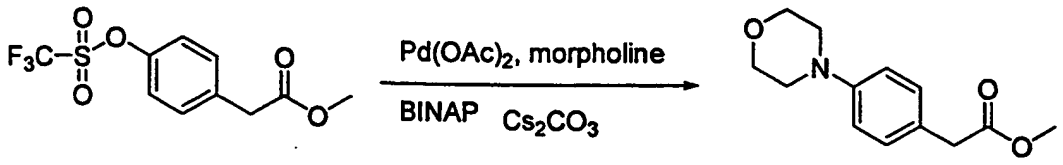
Prepared according to the general procedure outlined in Schemes 1 and 2. The starting materials were prepared as follows:

Methyl-4-(trifluoromethylsulfonyloxy)phenyl acetate



To methyl-4-hydroxyphenyl acetate (20 g, 120 mmol) and pyridine (20 mL, 240 mmol) in 100 mL dichloromethane at 0°C was added trifluoromethanesulfonic anhydride (23 mL, 132 mmol) dropwise over 30 minutes. After an additional 30 minutes at 0°C followed by 30 minutes at ambient temperature, 1N hydrochloric acid was added and the reaction mixture was extracted into dichloromethane. The organic layer was washed with 1N hydrochloric acid, saturated sodium bicarbonate, brine, dried over magnesium sulfate, filtered, and concentrated providing 32 g (90%) of the title compound as a yellow solid. ^{1}H NMR ($CDCl_3$; 300 MHz) δ 7.38 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 8.5 Hz, 2H), 3.72 (s, 3H), 3.66 (s, 2H).

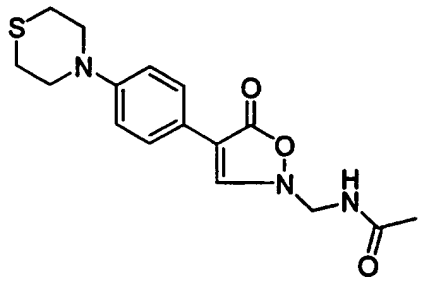
Methyl-4-morpholinophenyl acetate



Nitrogen was bubbled through a mixture of methyl-4-(trifluoromethylsulfonyloxy)phenyl acetate (1.0 g, 3.35 mmol), cesium carbonate (1.6 g, 4.69 mmol), palladium (II) acetate (22 mg, 0.10 mmol), (S)-BINAP (93 mg, 0.15 mmol), and morpholine (0.35 mL, 4.02 mmol) in 8 mL toluene and the reaction mixture was heated to 80°C for 6 hours. The reaction was then cooled, celite was added, and the mixture was concentrated. Chromatography was performed on a Biotage flash 40i chromatography module by loading the dried celite into a SIM and eluting with 20% ethyl acetate / hexanes (40S cartridge) providing 250 mg (37%) of the title compound as a yellow oil. ^{1}H NMR ($CDCl_3$; 300 MHz) δ 7.19 (d, J = 8.4 Hz, 2H), 6.87 (d, J = 8.3 Hz, 2H), 3.89-3.85 (m, 4H), 3.69 (s, 3H), 3.56 (s, 2H), 3.17-3.13 (m, 4H).

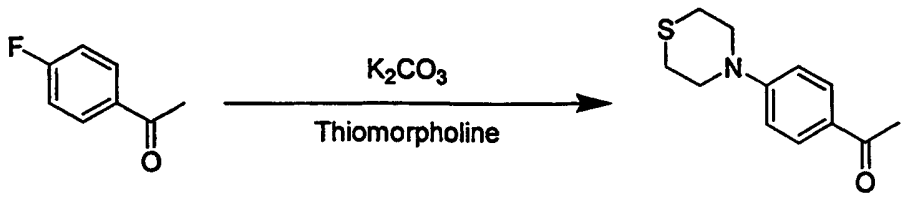
EXAMPLE 28

N-{[4-(4-(1,4-thiazaperhydroin-4-yl)phenyl)-5-oxo-2-hydroisoxazol-2-yl]methyl}acetamide



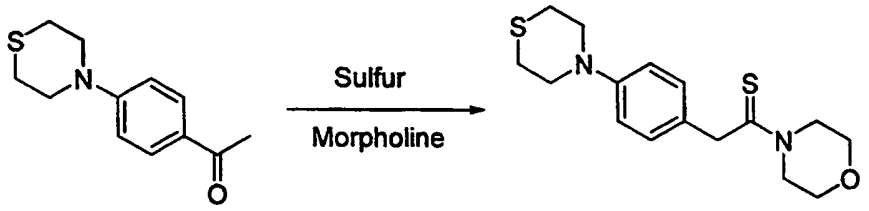
Prepared according to the general procedures outlined in Schemes 1 and 3. The starting materials were prepared as follows:

4-Thiomorpholinoacetophenone



To 4-fluoroacetophenone (20 g, 145 mmol) in 100 mL dimethylformamide was added potassium carbonate (39 g, 580 mmol) followed by thiomorpholine (87 mL, 870 mmol). The reaction mixture was heated to reflux and after 24 hours, it was cooled to ambient temperature and partitioned between water and dichloromethane. The organic layer was dried over magnesium sulfate, filtered, and concentrated. The residue was dissolved in ether and precipitated with hexanes providing 31 g (96%) of the title compound as a yellow solid. ^{1}H NMR ($CDCl_3$; 300 MHz) δ 7.87 (d, J = 9.0 Hz, 2H), 6.82 (d, J = 9.0 Hz, 2H), 3.81-3.78 (m, 4H), 2.73-2.69 (m, 4H), 2.53 (s, 3H).

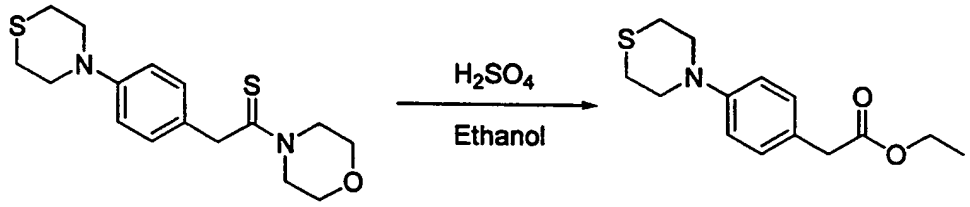
4-Thiomorpholinophenylthioacetomorpholide



A mixture of 4-thiomorpholinoacetophenone (30 g, 136 mmol), morpholine (16 mL, 180 mmol) and sulfur (6 g, 180 mmol) was heated to reflux for 6 hours, cooled to 50°C, and 100 mL 1:1 hexanes:ethyl acetate was added. The reaction mixture was again brought to reflux for 30 minutes, cooled, and the resultant orange precipitate was collected via filtration. The precipitate was washed with additional 1:1 ether / hexanes

providing 31 g (73%) of the title compound as a yellow-orange solid. ^{1}H NMR ($CDCl_3$; 300 MHz) δ 7.21 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.1 Hz, 2H), 4.35 (t, *J* = 4.8 Hz, 2H), 4.27 (s, 2H), 3.74 (t, *J* = 4.8 Hz, 2H), 3.65 (t, *J* = 4.2 Hz, 2H), 3.52 (t, *J* = 5.1 Hz, 4H), 3.41 (t, *J* = 5.4 Hz, 2H), 2.77-2.71 (m, 2H).

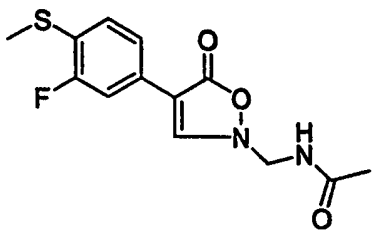
Ethyl-4-thiomorpholinophenyl acetate



A solution of 4-thiomorpholinophenylthioacetomorpholide (30 g, 93.2 mmol) in 70 mL 1:1 ethanol:sulfuric acid was heated to reflux for 18 hours, cooled to room temperature and solid sodium bicarbonate was slowly added to the reaction until it reached pH 7. The reaction mixture was extracted with chloroform, and the organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated to a yellow residue. The residue was then dissolved in chloroform, loaded onto a Biotage flash 40i chromatography module (40M cartridge) and chromatographed with 10% ethyl acetate / hexanes providing 12 g (51%) of the title compound as a yellow oil. ^{1}H NMR ($CDCl_3$; 300 MHz) δ 7.18 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 4.14 (q, *J* = 7.2 Hz, 2H), 3.54-3.50 (m, 6H), 2.76-2.73 (m, 4H), 1.25 (t, *J* = 7.2 Hz, 3H).

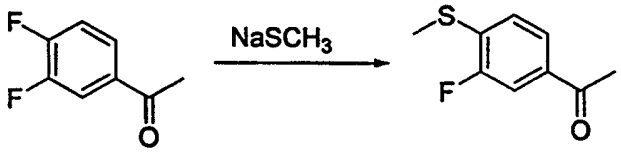
EXAMPLE 29

N-{[4-(3-fluoro-4-methylthiophenyl)-5-oxo-2-hydroisoxazol-2-yl]methyl}acetamide



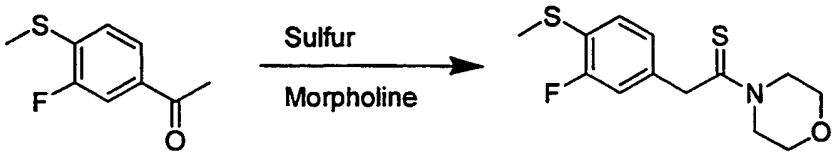
Prepared according to the general procedures outlined in Schemes 1 and 3. The starting materials were prepared as follows:

3-Fluoro-4-methylthioacetophenone



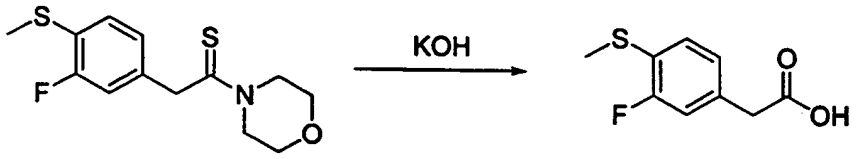
To 3, 4-difluoroacetophenone (30 g, 192 mmol) in 200 mL dimethylsulfoxide was added sodium thiomethoxide (15 g, 211 mmol). The reaction mixture was heated to 150°C for 2 hours and then partitioned between ethyl acetate and sodium bicarbonate. The organic layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated. The residue was dissolved in ethyl acetate and precipitated with hexanes. The precipitate was collected by filtration providing 25 g (70%) of the title compound as a yellow solid.

3-Fluoro-4-methylthiophenylthioacetomorpholide



A mixture of 3-fluoro-4-methylthioacetophenone (9.0 g, 48.9 mmol), morpholine (5.7 mL, 65.0 mmol), and sulfur (2.1 g, 65.0 mmol) were heated to reflux for 4 hours, cooled to 50°C, and 1:1 hexanes : ethyl acetate was added. The reaction mixture was again heated to reflux for 30 minutes, cooled to ambient temperature, and the resultant orange precipitate was collected by filtration. The precipitate was washed with 1:1 hexanes : ether providing 10.1 g (73%) of the title compound as a yellow-orange solid. ^{1}H NMR (DMSO-d_6; 300 MHz) δ 7.36-7.29 (m, 1H), 7.20-7.15 (m, 2H), 4.27 (s, 2H), 4.22 (t, J = 4.8 Hz, 2H), 3.73 (t, J = 4.5 Hz, 2H), 3.65 (t, J = 4.8 Hz, 2H), 3.47 (t, J = 5.1 Hz, 2H), 2.47 (s, 3H).

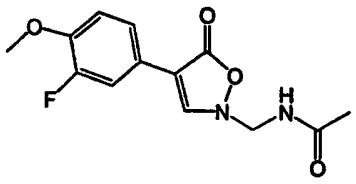
3-Fluoro-4-methylthiophenylacetic acid



To 3-fluoro-4-methylthiophenylthioacetomorpholide (2.6 g, 90.9 mmol) was added 500 mL 10% potassium hydroxide. The reaction mixture was heated to reflux for 3 hours, cooled to ambient temperature, and adjusted to pH 4 by the careful addition of 2N hydrochloric acid. The aqueous solution was extracted with dichloromethane and the organic layer was then extracted with 200 mL 10% potassium hydroxide. The aqueous layer was then brought to pH 4 by the careful addition of 2N hydrochloric acid and extracted with dichloromethane. The organic layer was dried over magnesium sulfate, filtered, and concentrated providing 10.0 g (55%) of the title compound as a brown oil. ^{1}H NMR ($CDCl_3$; 300 MHz) δ 7.24-7.21 (m, 1H), 7.04-6.99 (m, 2H), 3.63 (s, 2H), 2.46 (s, 3H).

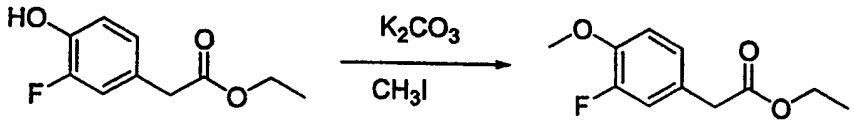
EXAMPLE 30

N-{[4-(3-fluoro-4-methoxyphenyl)-5-oxo-2-hydroisoxazol-2-yl]methyl}acetamide



Prepared according to the general procedure outlined in Schemes 1. The starting material was prepared as follows:

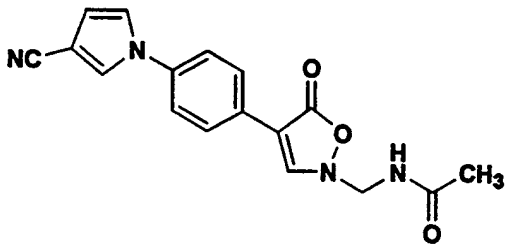
Ethyl-(3-Fluoro-4-methoxy)phenyl acetate



To ethyl-(3-fluoro-4-hydroxy)phenyl acetate (2.5 g, 8.9 mmol) in 20mL acetone was added potassium carbonate (3.4 g, 24.2 mmol) and iodomethane (1.5 mL, 24.2 mmol). The reaction mixture was heated to reflux for 2 hours, cooled, and partitioned between saturated sodium bicarbonate and ether. The organic layer was washed with brine, dried over magnesium sulfate, filtered and concentrated providing 2.3 g (88%) of the title compound as a yellow oil. ^{1}H NMR ($CDCl_3$; 300 MHz) δ 7.06-6.88 (m, 3H), 4.15 (q, J = 7.2 Hz, 2H), 3.88 (s, 3H), 3.54 (s, 2H), 1.26 (t, J = 7.2 Hz, 3H).

EXAMPLE 31

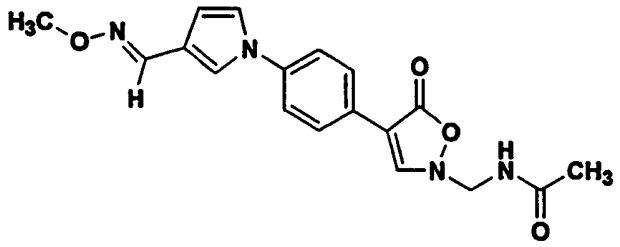
N-({4-[4-(3-cyanopyrrolyl)phenyl]-5-oxo-2-hydroisoxazol-2-yl}methyl)acetamide



To a mixture of N-[(4-{4-[3-((hydroxyimino)methyl)pyrrolyl]phenyl}-5-oxo-2-hydroisoxazol-2-yl)methyl]acetamide (100 mg, 0.29 mmol) in 3 ml of CH_3CN and 1 ml of CCl_4 was added polymer-bound triphenylphosphine (400 mg, 1.2 mmol) and the mixture was heated at reflux for 8 hours. It was then dissolved in ethyl acetate, filtered, and concentrated to yield a yellow solid. This solid was then triturated with ether to obtain 30 mg (32 %) of the title compound as a yellow solid. ^1H NMR (300 MHz, DMSO-d_6) δ 9.08 (s, 1 H), 8.97 (t, J = 6 Hz, 1 H), 8.28, (s, 1 H), 7.92 (d, J = 9 Hz, 2 H), 7.70 (d, J = 9 Hz, 2 H), 7.59 (m, 1 H), 6.74 (m, 1 H), 5.06 (d, J = 6 Hz, 2 H), 1.86 (s, 3 H).

EXAMPLE 32

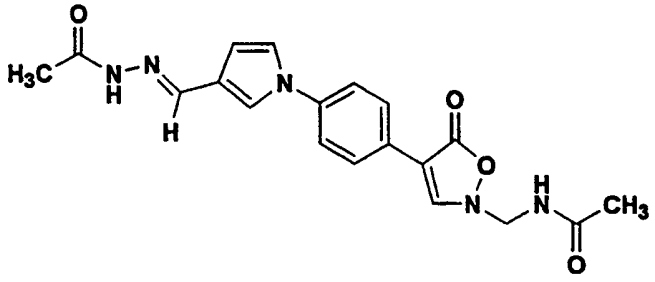
N-[(4-{4-[3-((1E)-2-aza-2-methoxyvinyl)pyrrolyl]phenyl}-5-oxo-2-hydroisoxazol-2-yl)methyl]acetamide



A mixture of N-({4-[4-(3-formylpyrrolyl)phenyl]-5-oxo-2-hydroisoxazol-2-yl}methyl)acetamide (100 mg, 0.3 mmol), $HCl \cdot NH_2OCH_3$ (31 mg, 0.37 mmol) and sodium carbonate (20 mg, 0.19 mmol) was dissolved in 3 mL of MeOH and 2 mL of water. To this mixture was added acetic acid to adjust the pH to 5. The reaction was heated at reflux for 1 hour. The reaction was cooled to room temperature, and the yellow precipitate was collected by filtration to give 40 mg (36 %) of the title compound as a yellow solid. $(M+H^+)= 355$.

EXAMPLE 33

N-{[4-(4-{3-[(1E)-2-(acetylamino)-2-azavinyl]pyrrolyl}phenyl)-5-oxo-2-hydroisoxazol-2-yl]methyl}acetamide

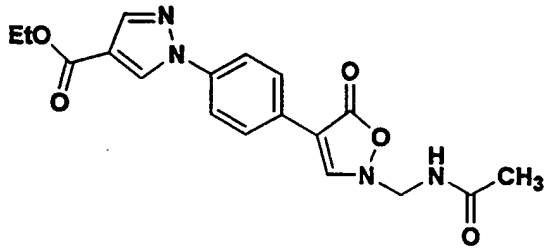


A mixture of N-({4-[4-(3-formylpyrrolyl)phenyl]-5-oxo-2-hydroisoxazol-2-yl]methyl)acetamide (100 mg, 0.30 mmol) and acetic hydrazide (28 mg, 0.38 mmol) in 3 mL of EtOH was heated at reflux for 1 hour. The reaction was cooled to room temperature, and the yellow

precipitate was collected by filtration to give 80mg (36 %) of the title compound. $(M+H^+)=382$.

EXAMPLE 34

Ethyl 1-(4-{2-[(acetylamino)methyl]-5-oxo-2-hydroisoxazol-4-yl}phenyl)pyrazole- 4-carboxylate



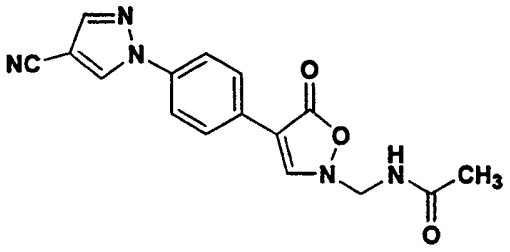
To a mixture of N-{[4-(4-hydrazinylphenyl)-5-oxo-2-hydroisoxazol-2-yl]methyl}acetamide hydrochloride (150 mg, 0.5 mmol) in 3 mL of methanol was added sodium bicarbonate (50 mg, 0.6 mmol) and ethoxycarbonylmalondialdehyde (75 mg, 0.52 mmol). The mixture was stirred at room temperature overnight. The solid was collected by filtration and then washed with water, and dried to yield 140 mg of a purple solid. The crude product was subjected to silica gel chromatography (eluting with ethyl acetate followed by 5% methanol/ethyl acetate) to yield 123 mg (66%) of the title compound as a yellow solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.11 (s, 1 H), 9.08 (s, 1 H), 8.96 (t, J = 6 Hz, 1 H), 8.15 (s, 1 H), 7.95 (m, 4 H), 5.06 (d, J = 6 Hz, 2 H), 4.28, (q, J = 7 Hz, 2 H), 1.86 (s, 3 H), 1.31 (t, J = 7 Hz, 3 H).

The starting material, N-{[4-(4-hydrazinylphenyl)-5-oxo-2-hydroisoxazol-2-yl]methyl}acetamide hydrochloride, was prepared as follows. Sodium nitrite (112 mg, 1.6 mmol) in 2 mL of water was added to a solution of N-{[4-(4-aminophenyl)-5-oxo-2-hydroisoxazol-2-yl]methyl}acetamide (400 mg, 1.6 mmol) in concentrated hydrochloric acid

at 0°C over 5 minutes. The reaction was stirred for an additional 10 minutes at 0°C, and then $SnCl_2 \cdot 2H_2O$ (720 mg, 3.2 mmol) in 2 mL of concentrated hydrochloric acid was added. This mixture was stirred at room temperature for 3 hours. The reaction mixture was then filtered to collect a yellow solid which was washed with 3 mL of water and dried to yield 260 mg (55%) of the title compound. ^1H NMR (300 MHz, DMSO-d_6) δ 10.2 (s, 2 H), 8.94 (t, J = 6 Hz, 1 H), 8.82, (s, 1 H), 8.35 (s, 1 H), 7.70 (d, J = 9, 2 H), 6.99 (d, J = 9, 2 H), 4.99 (d, J = 6 Hz, 2 H), 1.84 (s, 3 H).

EXAMPLE 35

N-({4-[4-(4-cyanopyrazolyl)phenyl]-5-oxo-2-hydroisoxazol-2-yl}methyl)acetamide

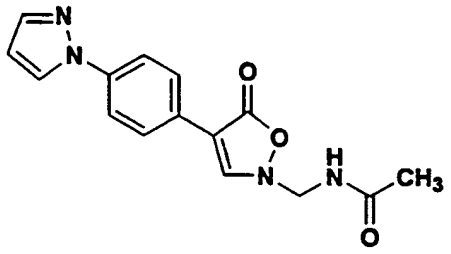


To a mixture of N-{[4-(4-hydrazinylphenyl)-5-oxo-2-hydroisoxazol-2-yl]methyl}acetamide hydrochloride (50 mg, 0.17 mmol) in 2 mL of methanol was added 20 mg (0.24 mmol) of sodium bicarbonate and cyanomalondialdehyde (30 mg, 0.3 mmol). The mixture was stirred at room temperature overnight. It was then concentrated to give a solid which was washed with water then methanol to give 42 mg (76%) of the title compound as a yellow solid. ^1H NMR (300 MHz, DMSO-d_6) δ 9.35 (s, 1 H), 9.10 (s, 1 H), 8.98 (t, J = 6 Hz, 1 H), 8.37 (s, 1 H), 7.93 (m, 4 H), 5.07 (d, J = 6 Hz, 2 H), 1.86 (s, 3 H).

Preparation of cyanomalondialdehyde. To a dried flask was added sodium hydride (0.82 g, 50% suspended in mineral oil, 17 mmol). The sodium hydride was washed three times with 15 mL of ether, and then 15 mL of ether was added to the flask. After cooling the slurry to 0°C, ethyl formate (10.4 g, 140 mmol) was added. To this mixture was added 3,3-diethoxypropionitrile (2 g, 14 mmol) in 10 ml of ether over 2 hours (syringe pump). The mixture was stirred at room temperature for 20 hours, and then poured into 100 mL of ice water. This solution was extracted three times with ether, and then the ether extracts were discarded. The aqueous phase was acidified to pH 3 with concentrated HCl and extracted with dichloromethane. The organic phase was dried over $MgSO_4$, filtered, and concentrated to yield 0.3 g of cyanomalondialdehyde as a yellow solid. Additional product was recovered from the pH 3 aqueous phase: the aqueous phase was concentrated to dryness, and then dissolved in 5 mL of methanol. The inorganic salt was removed by filtration, and the filtrate was concentrated to yield 1 g of cyanomalondialdehyde as a yellow solid. ^1H NMR (300 MHz, DMSO-d_6) δ 8.94 (s, 2 H), 4.95 (br s, 1 H).

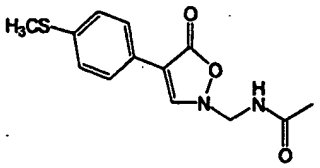
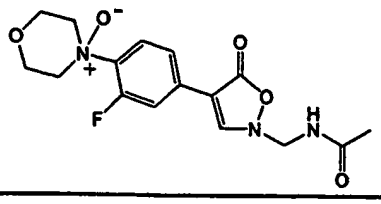
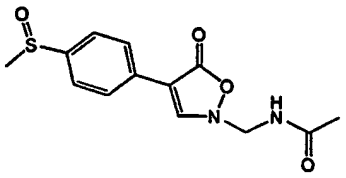
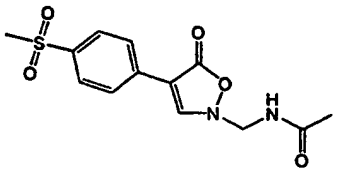
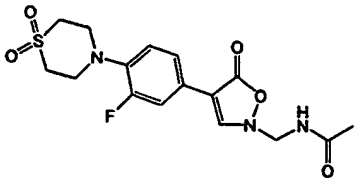
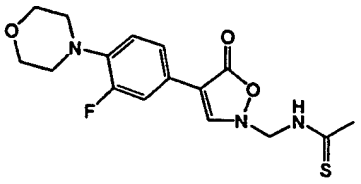
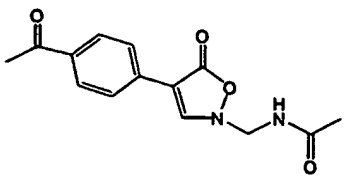
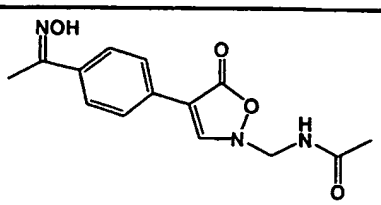
EXAMPLE 36

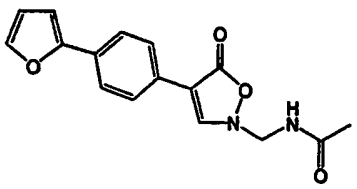
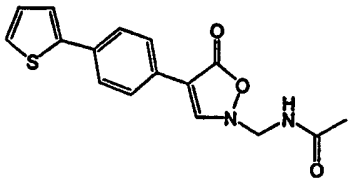
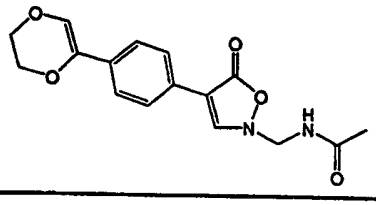
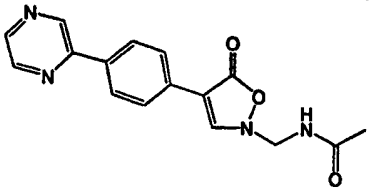
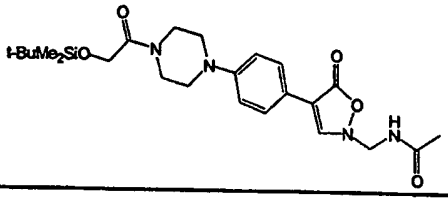
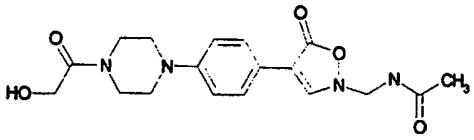
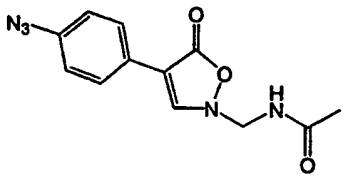
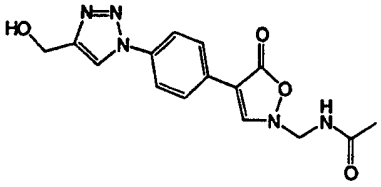
N-{[5-oxo-4-(4-pyrazolylphenyl)-2-hydroisoxazol-2-yl]methyl}acetamide

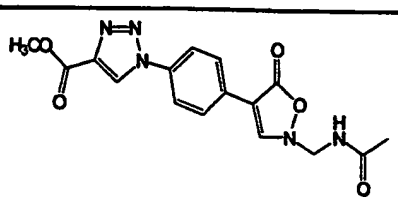
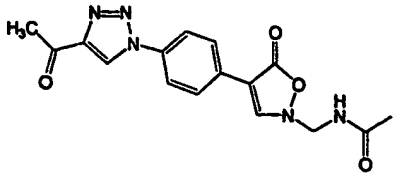
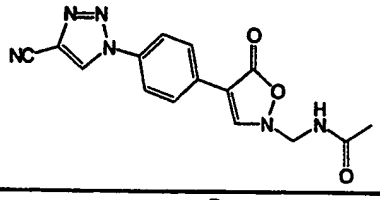
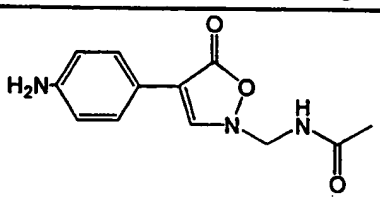
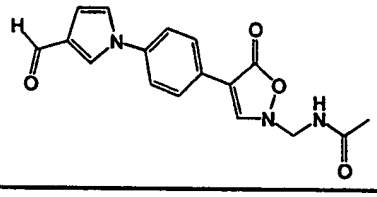
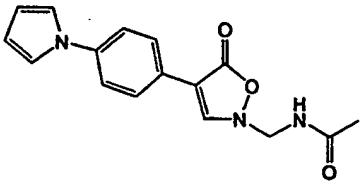
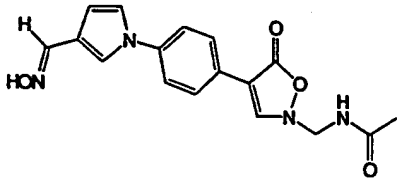
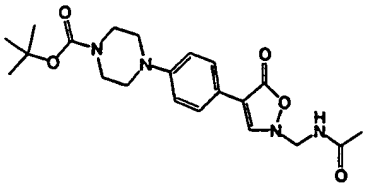


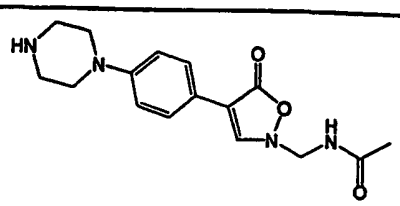
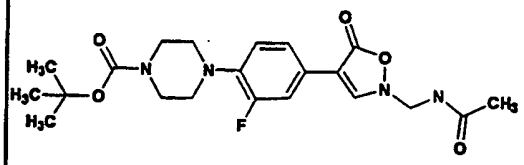
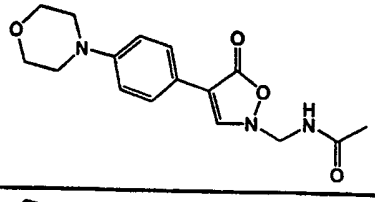
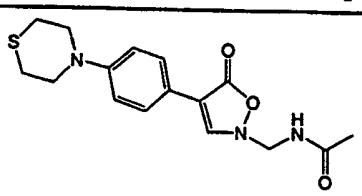
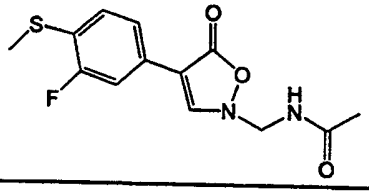
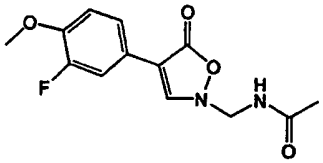
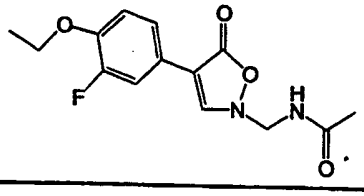
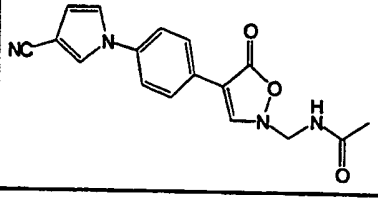
To a mixture of N-{[4-(4-hydrazinylphenyl)-5-oxo-2-hydroisoxazol-2-yl]methyl}acetamide hydrochloride (100 mg, 0.33 mmol) in 3 mL of methanol was added sodium bicarbonate (28 mg, 0.33mmol) and malondialdehyde (50 mg, 0.35 mmol). The mixture was stirred at room temperature overnight. It was then concentrated to yield 120 mg of a yellow oil, which was then purified by silica gel chromatography (eluting with ethyl acetate) to obtain 30 mg (30%) of the title compound as a yellow solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.03 (s, 1 H), 8.95 (t, J = 6 Hz, 1 H), 8.52 (s, 1 H), 7.88 (m, 4 H), 7.75 (s, 1 H), 6.56 (s, 1 H), 5.05 (d, J = 6 Hz, 2 H), 1.86 (s, 3 H).

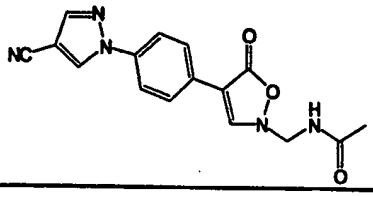
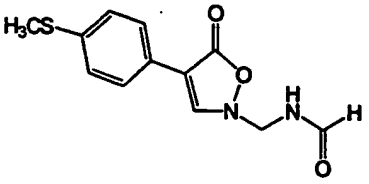
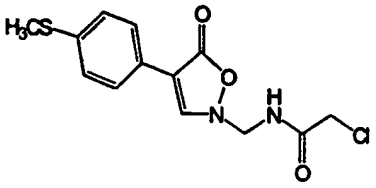
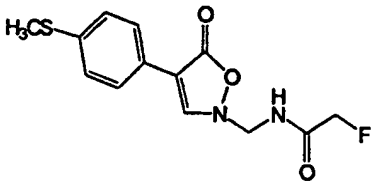
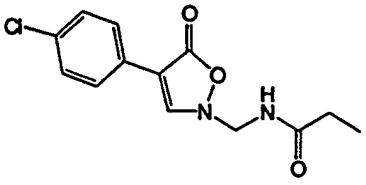
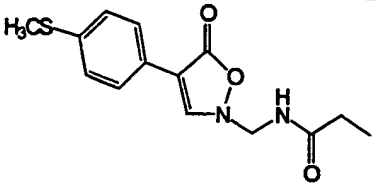
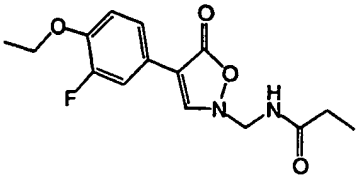
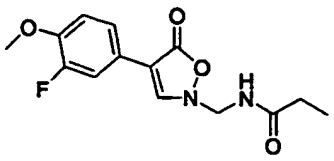
The table below shows the chemical structures, characterizing properties (MS data) and preparative method for several representative compounds of the present invention, including those of Examples 1-36 described above.

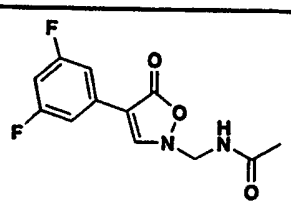
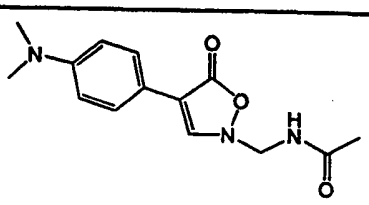
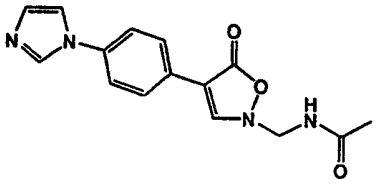
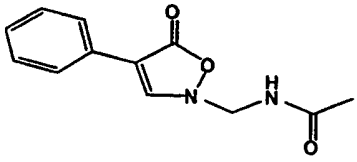
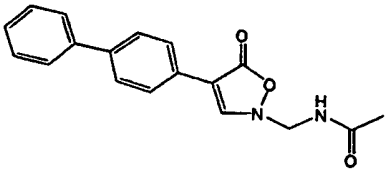
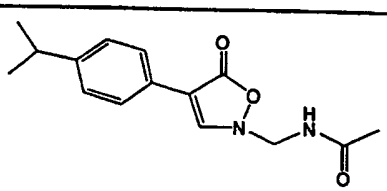
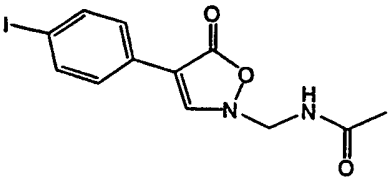
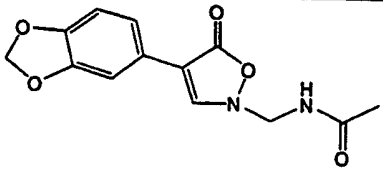
	Structure	MS data	Prepared via Scheme(s)
1		(M+H)+ = 279 ESI	1
2		(M+H)+ = 352 DCI	3, 1
3		(M+H)+ = 295 ESI	1, 4
4		(M+H)+ = 311 ESI	1, 4
5		(M+H)+ = 384 ESI	3, 1, 4
6		(M+H)+ = 352 ESI	3, 1, 9
7		(M+H)+ = 275 ESI	1
8		(M+H)+ = 290 ESI	1

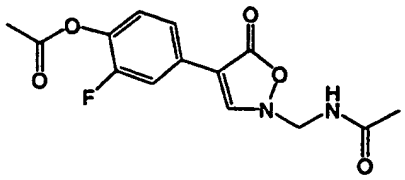
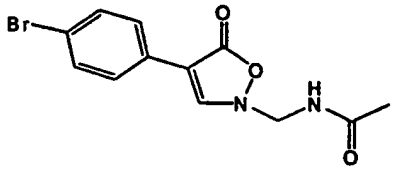
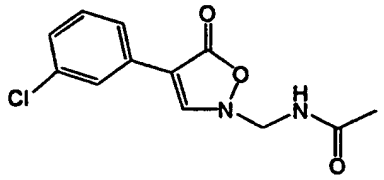
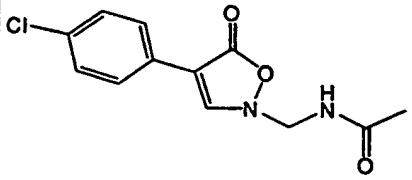
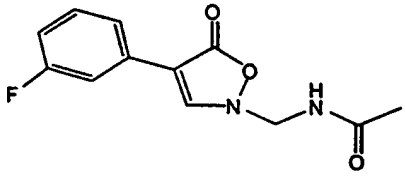
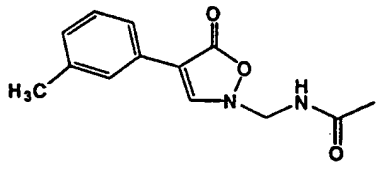
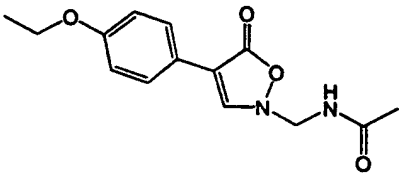
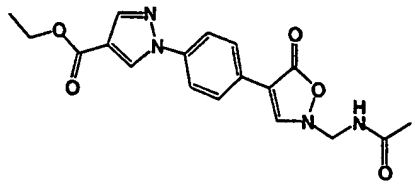
	Structure	MS data	Prepared via Scheme(s)
9		(M+H)+ = 299 ESI	1, 5
10		(M+H)+ = 315 ESI	1, 5
11		(M+H)+ = 317 ESI	1, 5
12		(M+H)+ = 311 ESI	1, 5
13		(M+H)+ = 489 ESI	2, 1, 6
14		(M+H)+ = 375 ESI	2, 1, 6
15		(M+H)+ = 274 DCI	1
16		(M+H)+ = 330 ESI	1, 7

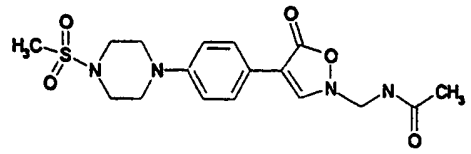
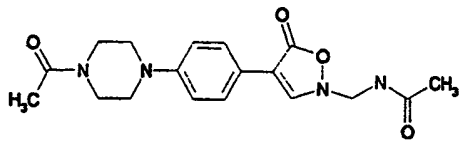
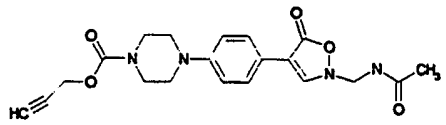
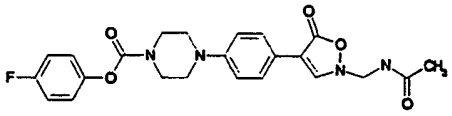
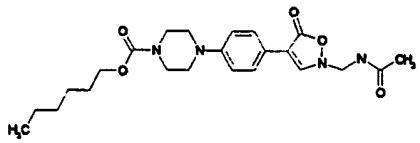
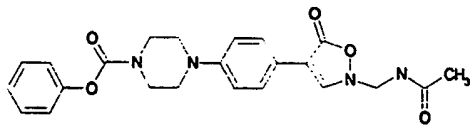
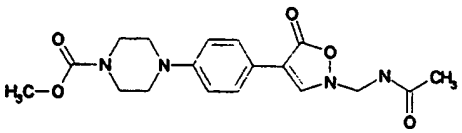
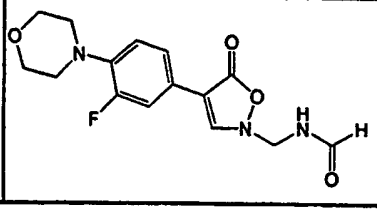
	Structure	MS data	Prepared via Scheme(s)
17		(M+H)+ = 358 ESI	1, 7
18		(M+H)+ = 342 DCI	1, 7
19		(M+H)+ = 325 DCI	1, 7
20		(M+H)+ = 248 DCI	1, 8
21		(M+H)+ = 326 DCI	1, 8
22		(M+H)+ = 298 ESI	1, 8
23		(M+H)+ = 341 ESI	1, 8
24		(M+H)+ = 417 ESI	2, 1, 6

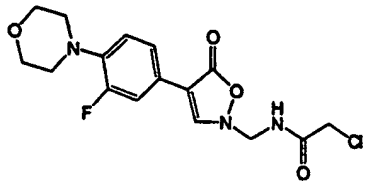
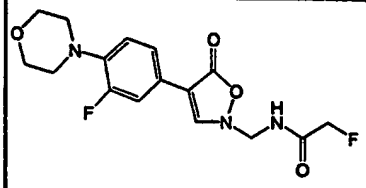
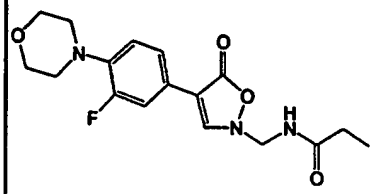
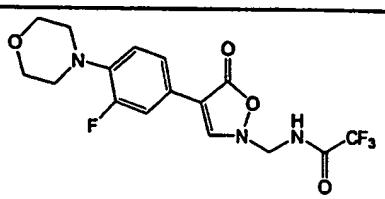
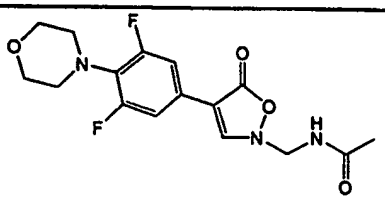
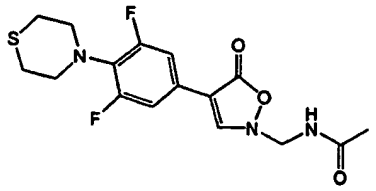
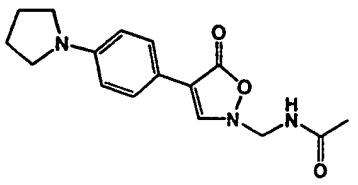
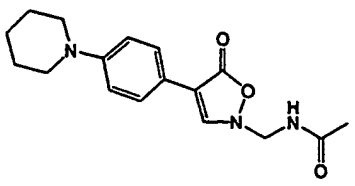
	Structure	MS data	Prepared via Scheme(s)
25		(M+H)+ = 317 ESI	2, 1, 6
26		(M+H)+ = 435 ESI	3, 1, 6
27		(M+H)+ = 318 ESI	2, 1
28		(M+H)+ = 334 ESI	3, 1
29		(M+H)+ = 297 DCI	3, 1
30		(M+H)+ = 281 ESI	3, 1
31		(M+H)+ = 295 ESI	3, 1
32		(M+H)+ = 323 ESI	1, 8

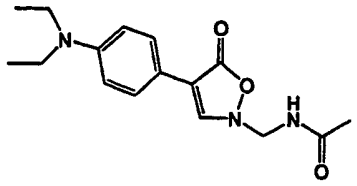
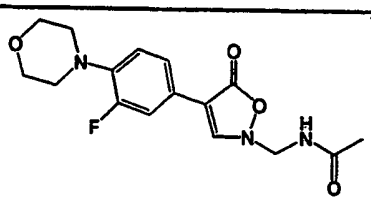
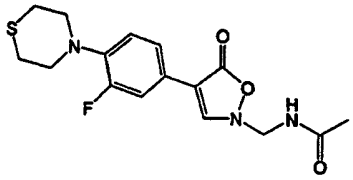
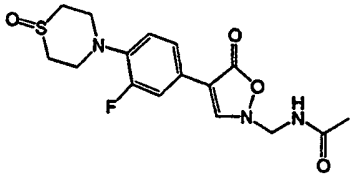
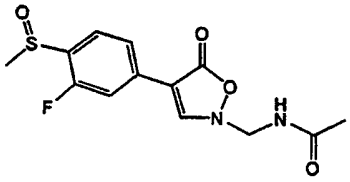
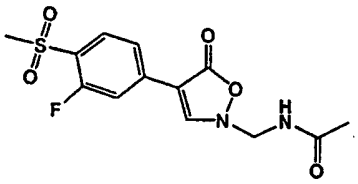
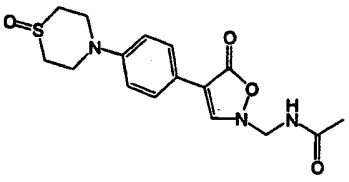
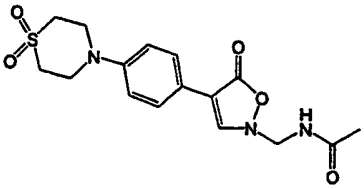
	Structure	MS data	Prepared via Scheme(s)
33		(M+H)+ = 324 DCI	1,8
34		(M+H)+ = 265 DCI	1
35		(M+H)+ = 313 DCI	1
36		(M+H)+ = 297 DCI	1
37		(M+H)+ = 281 ESI	1
38		(M+H)+ = 293 ESI	1
39		(M+H)+ = 309 ESI	1
40		(M+H)+ = 295 ESI	1

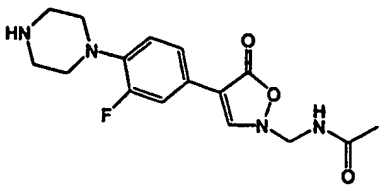
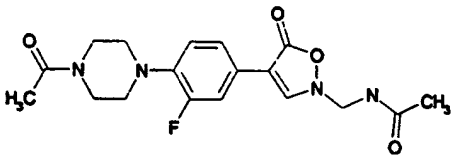
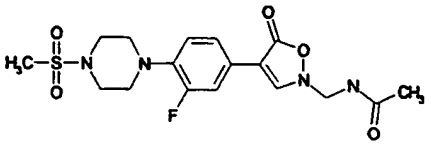
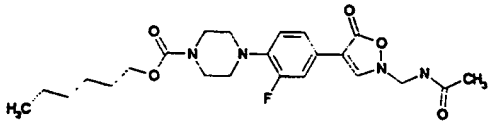
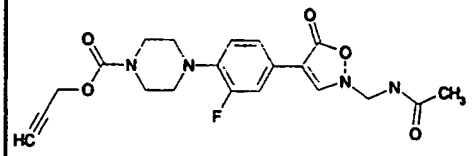
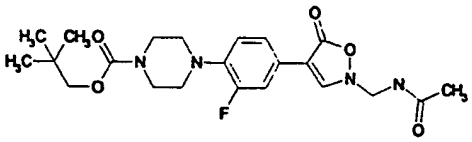
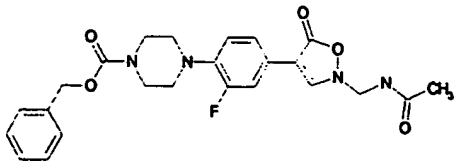
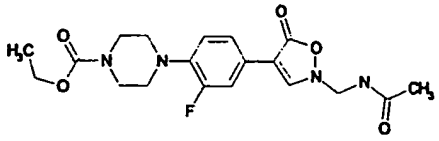
	Structure	MS data	Prepared via Scheme(s)
41		(M+H)+ = 369 DCI	1
42		(M+H)+ = 276 ESI	1
43		(M+H)+ = 299 ESI	1
44		(M+H)+ = 233 ESI	1
45		(M+H)+ = 309 ESI	1
46		(M+H)+ = 275 ESI	1
47		(M+H)+ = 359 ESI	1
48		(M+H)+ = 277 ESI	1

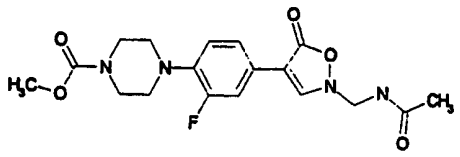
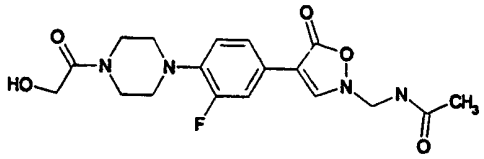
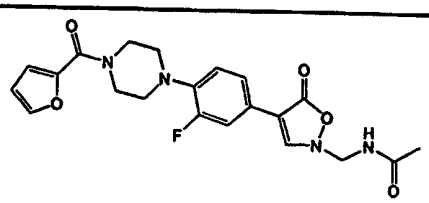
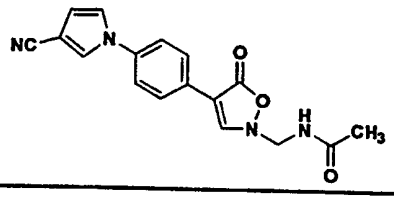
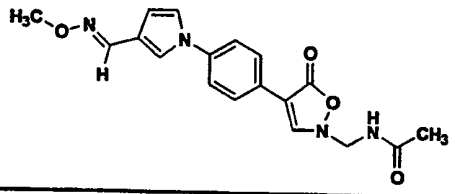
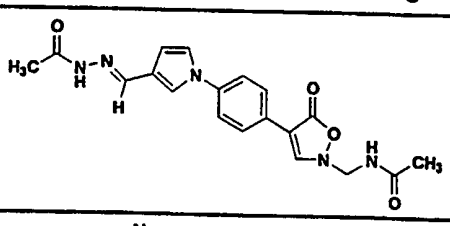
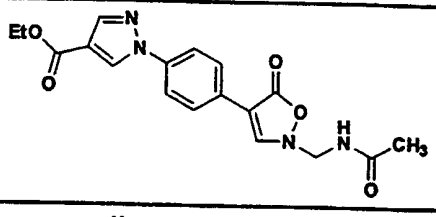
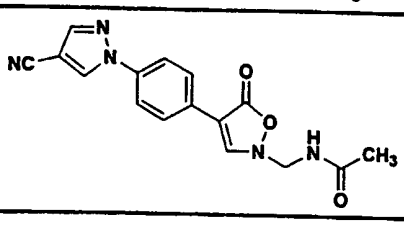
	Structure	MS data	Prepared via Scheme(s)
49		(M+H)+ = 309 ESI	1
50		(M+H)+ = 312 ESI	1
51		(M+H)+ = 268 ESI	1
52		(M+H)+ = 268 ESI	1
53		(M+H)+ = 251 ESI	1
54		(M+H)+ = 247 ESI	1
55		(M+H)+ = 277 ESI	1
56		(M+H)+ = 371 DCI	1,8

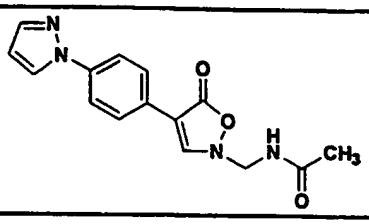
	Structure	MS data	Prepared via Scheme(s)
57		(M+H)+ = 395 ESI	2, 1, 6
58		(M+H)+ = 359 ESI	2, 1, 6
59		(M+H)+ = 399 ESI	2, 1, 6
60		(M+H)+ = 455 ESI	2, 1, 6
61		(M+H)+ = 445 ESI	2, 1, 6
62		(M+H)+ = 437 ESI	2, 1, 6
63		(M+H)+ = 375 ESI	2, 1, 6
64		(M+H)+ = 322 ESI	3, 1

	Structure	MS data	Prepared via Scheme(s)
65		(M+H)+ = 370 ESI	3, 1
66		(M+H)+ = 354 ESI	3, 1
67		(M+H)+ = 350 ESI	3, 1
68		(M+H)+ = 390 ESI	3, 1
69		(M+H)+ = 354 ESI	3, 1
70		(M+H)+ = 370 ESI	3, 1
71		(M+H)+ = 302 ESI	3, 1
72		(M+H)+ = 316 ESI	3, 1

	Structure	MS data	Prepared via Scheme(s)
73		(M+H)+ = 304 ESI	3, 1
74		(M+H)+ = 336 ESI	3, 1
75		(M+H)+ = 352 ESI	3, 1
76		(M+H)+ = 368 ESI	3, 1, 4
77		(M+H)+ = 313 ESI	3, 1, 4
78		(M+H)+ = 329 ESI	3, 1, 4
79		(M+H)+ = 350 ESI	3, 1, 4
80		(M+H)+ = 366 ESI	3, 1, 4

	Structure	MS data	Prepared via Scheme(s)
81		(M+H)+ = 334 ESI	3, 1, 6
82		(M+H)+ = 377 ESI	3, 1, 6
83		(M+H)+ = 413 ESI	3, 1, 6
84		(M+H)+ = 463 ESI	3, 1, 6
85		(M+H)+ = 417 ESI	3, 1, 6
86		(M+H)+ = 449 ESI	3, 1, 6
87		(M+H)+ = 469 ESI	3, 1, 6
88		(M+H)+ = 407 ESI	3, 1, 6

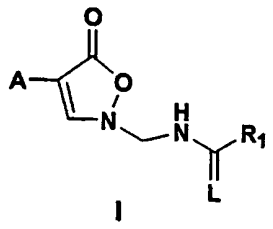
	Structure	MS data	Prepared via Scheme(s)
89		(M+H)+ = 393 ESI	3, 1, 6
90		(M+H)+ = 393 ESI	3, 1, 6
91		(M+H)+ = 429 ESI	3, 1, 6
92		(M+H)+ = 323 ESI	1, 8
93		(M+H)+ = 355 ESI	1, 8
94		(M+H)+ = 382 ESI	1, 8
95		(M+H)+ = 371 DCI	1, 9
96		(M+H)+ = 324 DCI	1, 9

	Structure	MS data	Prepared via Scheme(s)
97		(M+H)+ = 299 ESI	1, 9

CLAIMS

We claim:

1. A compound of the formula



I

or a pharmaceutically acceptable salt thereof wherein:

R_1 is

a) H,

b) C_{1-8} alkyl optionally substituted with one or more F, Cl, OH, C_{1-8} alkoxy, or C_{1-8} acyloxy,

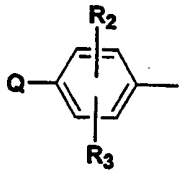
c) C_{3-6} cycloalkyl, or

d) C_{1-8} alkoxy;

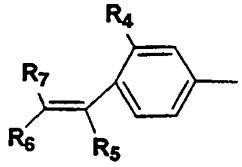
L is oxygen or sulfur;

A is

a)



b)

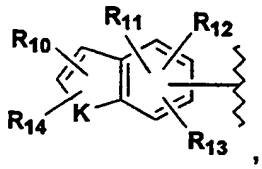


c) a 5-membered heteroaromatic moiety having one to three hetero atoms selected from the group consisting of S, N, and O, wherein the 5-membered heteroaromatic moiety is bonded via a carbon atom and can additionally have a fused-on benzene or naphthyl ring, and wherein the heteroaromatic moiety is optionally substituted with one to three R_8,

d) a 6-membered heteroaromatic moiety having at least one nitrogen atom, wherein the heteroaromatic moiety is bonded via a carbon atom, wherein the 6-membered heteroaromatic moiety can additionally have a fused-on benzene or naphthyl ring, wherein the heteroaromatic moiety is optionally substituted with one to three R_9,

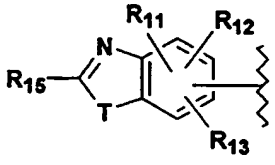
e) a β-carbolin-3-yl, or indolizinyl bonded via the 6-membered ring, optionally substituted with one to three R_9,

f)



, or

g)



;

wherein R_2 and R_3 are each independently

a) H,

b) F,

c) Cl,

d) Br,

e) C_{1-6} alkyl,

f) NO_2,

g) I,

h) C_{1-6} alkoxy,

i) OH

j) amino,

k) cyano, or

l) R_2 and R_3 taken together are $-O(CH_2)_h-O$;

wherein R_4 is

a) H,

b) C_{1-2} alkyl,

c) F, or

d) OH;

R_5 is

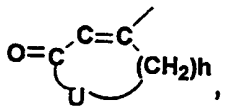
a) H,

b) CF_3,

c) C_{1-3} alkyl optionally substituted with one or more halo,

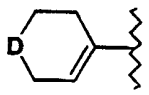
d) phenyl optionally substituted with one or more halo,

e) R_5 and R_6 taken together are a 5-, 6-, or 7-membered ring of the formula,



,

f)



in which D is S, O or NR_{86} in which R_{86} is H or C_{1-6} alkyl, or

g) R_5 and R_6 taken together are $-(CH_2)_k-$, when R_7 is an electron-withdrawing group;

R_6 and R_7 at each occurrence are the same or different and are

a) an electron-withdrawing group,

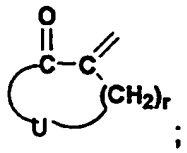
b) H,

c) CF_3,

d) C_{1-3} alkyl optionally substituted with one halo,

e) phenyl, provided at least one of R_6 and R_7 is an electron-withdrawing group, or

f) R_6 and R_7 taken together are a 5-, 6-, or 7-membered ring of the formula,



;

U is

a) CH_2,

b) O,

c) S or,

d) NR_{16};

R_{16} is

a) H or

b) C_{1-5} alkyl;

wherein R_8 is

a) carboxyl,

b) halo,

c) -CN,

d) mercapto,

e) formyl,

f) CF_3,

g) NO_2,

h) C_{1-6} alkoxy,

i) C_{1-6} alkoxycarbonyl,

j) C_{1-6} alkythio,

k) C_{1-6} acyl,

l) $-NR_{17}R_{18}$,

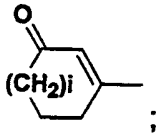
m) $-\overset{\overset{NOH}{\|}}{C}-R_{87}$ in which R_{87} is H or C_{1-6} alkyl,

n) C_{1-6} alkyl optionally substituted with OH, sulfamoyl, C_{1-5} alkoxy, C_{1-5} acyl, or $-NR_{17}R_{18}$,

o) C_{2-8} alkyl optionally substituted with one or two R_{19},

p) phenyl optionally substituted with one or two R_{19},

q) a 5- or 6-membered saturated or unsaturated heterocyclic moiety having one to three atoms selected from the group consisting of S, N, and O, optionally substituted with one or two R_{19}, or



;

R_{17} and R_{18} at each occurrence are the same or different and are

a) H,

b) C_{1-4} alkyl,

c) C_{5-6} cycloalkyl, or

d) R_{17} and R_{18} taken together with the nitrogen atom is a 5- or 6-membered saturated or unsaturated heterocyclic moiety which optionally has a further hetero atom selected from the group consisting of S, N, O, and can in turn be optionally substituted with, including on the further nitrogen atom, C_{1-3} alkyl, formyl, a 5- or 6-membered heteroaromatic moiety containing 1-3 O, N or S, $-\overset{\overset{O}{\|}}{C}-NR_{88}R_{89}$ in which R_{88} and R_{89} are each independently hydrogen or C_{1-6} alkyl, SO_2R_{90} in which R_{90} is H or C_{1-6} alkyl, or C_{1-3} acyl optionally substituted with 1 or more F, Cl or OH;

R_{19} is

a) carboxyl,

b) halo,

c) -CN,

d) mercapto,

e) formyl,

f) CF_3,

g) NO_2,

h) C_{1-6} alkoxy,

i) C_{1-6} alkoxycarbonyl,

j) C_{1-6} alkythio,

k) C_{1-6} acyl,

l) C_{1-6} alkyl optionally substituted with OH, C_{1-5} alkoxy, C_{1-5} acyl, or $-NR_{17}R_{18}$,

m) phenyl,

n) $-C(=O)NR_{20}R_{21}$,

o) $-N\ R_{17}R_{18}$,

p) $-N(R_{20})(-SO_2R_{22})$,

q) $-SO_2-NR_{20}R_{21}$, or

r) $-S(=O)_iR_{22}$;

R_{20} and R_{21} at each occurrence are the same or different and are

a) H,

b) C_{1-6} alkyl, or

c) phenyl;

R_{22} is

a) C_{1-4} alkyl, or

b) phenyl optionally substituted with C_{1-4} alkyl;

wherein R_9 is

a) carboxyl,

b) halo,

c) -CN,

d) mercapto,

e) formyl,

f) CF_3,

g) NO_2,

h) C_{1-6} alkoxy,

i) C_{1-6} alkoxycarbonyl,

j) C_{1-6} alkythio,

k) C_{1-6} acyl,

l) $-NR_{23}R_{24}$,

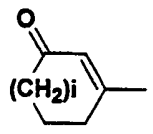
m) C_{1-6} alkyl optionally substituted with OH, C_{1-5} alkoxy, C_{1-5} acyl, or $-NR_{23}R_{24}$,

n) C_{2-8} alkenylphenyl optionally substituted with one or two R_{25},

o) phenyl optionally substituted with one or two R_{25},

p) a 5- or 6-membered saturated or unsaturated heterocyclic moiety having one to three atoms selected from the group consisting of S, N, and O, optionally substituted with one or two R_{25}, or

q)



,

R_{23} and R_{24} at each occurrence are the same or different and are

a) H,

b) formyl,

c) C_{1-4} alkyl,

d) C_{1-4} acyl,

e) phenyl,

f) C_{3-6} cycloalkyl, or

g) R_{23} and R_{24} taken together with the nitrogen atom is a 5- or 6-membered saturated heterocyclic moiety which optionally has a further hetero atom selected from the group consisting of S, N, O, and can in turn be optionally substituted with, including on the further nitrogen atom, phenyl, pyrimidyl, C_{1-3} alkyl, or C_{1-3} acyl;

R_{25} is

a) carboxyl,

b) halo,

c) -CN,

d) mercapto,

e) formyl,

f) CF_3,

g) NO_2,

h) C_{1-6} alkoxy,

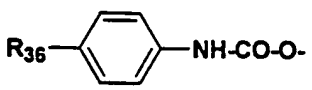
i) C_{1-6} alkoxycarbonyl,

j) C_{1-6} alkythio,

k) C_{1-6} acyl,

l) phenyl,

m) C_{1-6} alkyl optionally substituted with OH, azido, C_{1-5} alkoxy, C_{1-5} acyl, $-NR_{32}R_{33}$, $-SR_{34}$, $-O-SO_2R_{35}$, or



n) $-C(=O)NR_{26}R_{27}$,

o) $-NR_{23}R_{24}$,

p) $-N(R_{26})(-SO_2R_{22})$,

q) $-SO_2-NR_{26}R_{27}$, or

r) $-S(=O)_iR_{22}$,

s) $-CH=N-R_{28}$, or

t) $-CH(OH)-SO_3R_{31}$;

R_{22} is the same as defined above;

R_{26} and R_{27} at each occurrence are the same or different and are

a) H,

b) C_{1-6} alkyl,

c) phenyl, or

d) tolyl;

R_{28} is

a) OH,

b) benzyloxy,

c) $-NH-C(=O)-NH_2$,

d) $-NH-C(=S)-NH_2$, or

e) $-NH-C(=NH)-NR_{29}R_{30}$;

R_{29} and R_{30} at each occurrence are the same or different and are

a) H, or

b) C_{1-4} alkyl optionally substituted with phenyl or pyridyl;

R_{31} is

a) H, or

b) a sodium ion;

R_{32} and R_{33} at each occurrence are the same or different and are

a) H,

b) formyl,

c) C_{1-4} alkyl,

d) C_{1-4} acyl,

e) phenyl,

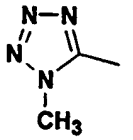
f) C_{3-6} cycloalkyl,

g) R_{32} and R_{33} taken together are a 5- or 6-membered saturated heterocyclic moiety having one to three atoms selected from the group consisting of S, N, O, optionally substituted with, including on the nitrogen atom, phenyl, pyrimidyl, C_{1-3} alkyl, or C_{1-3} acyl,

h) $-P(O)(OR_{37})(OR_{38})$, or

i) $-SO_2-R_{39}$;

R_{34} is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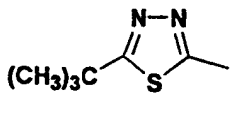
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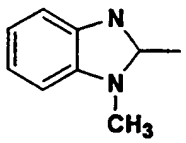
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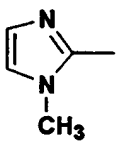

;

R_{35} is C_{1-3} alkyl;

R_{36} is

a) C_{1-6} alkoxycarbonyl, or

b) carboxyl;

R_{37} and R_{38} at each occurrence are the same or different and are

a) H, or

b) C_{1-3} alkyl;

R_{39} is

a) methyl,

b) phenyl, or

c) tolyl;

wherein K is

a) O,

b) S, or

c) NR_{40} in which R_{40} is hydrogen, formyl, C_{1-4} alkyl, C_{1-4} acyl, phenyl, C_{3-6} cycloalkyl, $-P(O)(OR_{37})(OR_{38})$ or $-SO_2-R_{39}$ in which R_{37}, R_{38} and R_{39} are as defined above;

R_{10}, R_{11}, R_{12}, R_{13}, R_{14} and R_{15} at each occurrence are the same or different and are

a) H,

b) formyl,

c) carboxyl,

d) C_{1-6} alkoxycarbonyl,

e) C_{1-8} alkyl,

f) C_{2-8} alkenyl,

wherein the substitutents (e) and (f) can be optionally substituted with OH, halo, C_{1-6} alkoxyl, C_{1-6} acyl, C_{1-6} alkylthio or C_{1-6} alkoxycarbonyl, or phenyl optionally substituted with halo,

g) an aromatic moiety having 6 to 10 carbon atoms optionally substituted with carboxyl, halo, -CN, formyl, CF_3, NO_2, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} acyl, C_{1-6} alkylthio, or C_{1-6} alkoxycarbonyl;

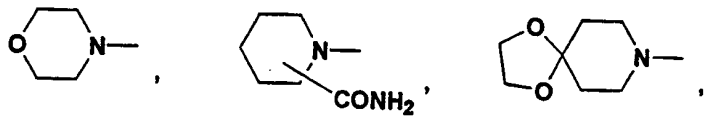
h) $-NR_{42}R_{43}$,

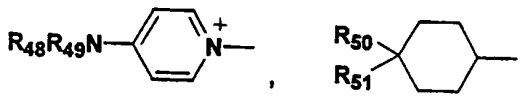
i) OR_{44},

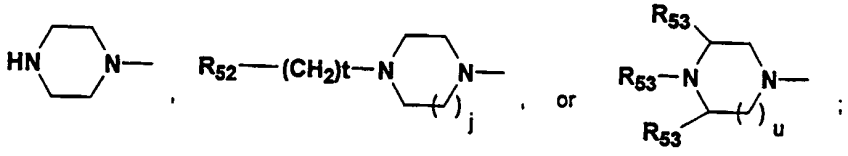
j) $-S(=O)_i-R_{45}$,

k) $-SO_2-N(R_{46})(R_{47})$, or

l) a radical of the following formulas:







R_{19} is the same as defined above;

T is

a) O,

b) S, or

c) SO_2;

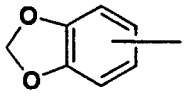
R_{42} and R_{43} at each occurrence are the same or different and are

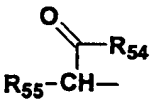
a) H,

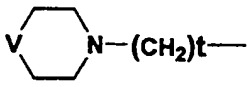
b) C_{3-6} cycloalkyl,

c) phenyl,

d) C_{1-6} acyl,

e) C_{1-8} alkyl optionally substituted with OH, C_{1-6} alkoxy which can be substituted with OH, a 5- or 6-membered aromatic heterocyclic moiety having one to three atoms selected from the group consisting of S, N, and O, phenyl optionally substituted with OH, CF_3, halo, $-NO_2$, C_{1-4} alkoxy,$-NR_{48}R_{49}$, or  ,

f)  , or

g)  ;

V is

a) O,

b) CH_2, or

c) NR_{56};

R_{48} and R_{49} at each occurrence are the same or different and are

a) H, or

b) C_{1-4} alkyl;

R_{54} is

a) OH,

b) C_{1-4} alkoxy, or

c) $-NR_{57}R_{58}$;

R_{55} is

a) H, or

b) C_{1-7} alkyl optionally substituted with indolyl, OH, mercaptyl, imidazoly, methylthio, amino, phenyl optionally substituted with OH, $-C(=O)-NH_2$, $-CO_2H$, or $-C(=NH)-NH_2$;

R_{56} is

a) H,

b) phenyl, or

c) C_{1-6} alkyl optionally substituted by OH;

R_{57} and R_{58} at each occurrence are the same or different and are

a) H,

b) C_{1-5} alkyl,

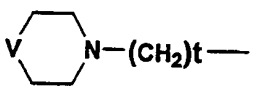
c) C_{1-3} cycloalkyl, or

d) phenyl;

R_{44} is

a) C_{1-8} alkyl optionally substituted with C_{1-6} alkoxy or C_{1-6} hydroxy, C_{3-6} cycloalkyl, a 6-membered aromatic optionally benzo-fused heterocyclic moiety having one to three nitrogen atoms, which can in turn be substituted with one or two $-NO_2$, CF_3, halo, -CN, OH, C_{1-5} alkyl, C_{1-5} alkoxy, or C_{1-5} acyl,

b)



c) phenyl, or

d) pyridyl;

R_{45} is

a) C_{1-16} alkyl,

b) C_{2-16} alkenyl,

wherein the substituents (a) and (b) can be optionally substituted with C_{1-6} alkoxycarbonyl, or a 5-, 6-, or 7-membered aromatic heterocyclic moiety having one to three atoms selected from the group consisting of S, N, and O,

c) an aromatic moiety having 6 to 10 carbon atoms, or

d) a 5-, 6-, or 7-membered aromatic heterocyclic moiety having one to three atoms selected from the group of S, N, and O, wherein the substituents (c) and (d) can be optionally substituted with carboxyl, halo, -CN, formyl, CF_3, $-NO_2$, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} acyl, C_{1-6} alkylthio, or C_{1-6} alkoxycarbonyl;

R_{46} and R_{47} at each occurrence are the same or different and are

a) H,

b) phenyl,

c) C_{1-6} alkyl, or

d) benzyl;

R_{50} and R_{51} at each occurrence are the same or different and are

a) H,

b) OH,

c) C_{1-6} alkyl optionally substituted with $-NR_{48}R_{49}$ in which R_{48} and R_{49} are as defined above,

d) R_{50} and R_{51} taken together are =O;

R_{52} is

a) an aromatic moiety having 6 to 10 carbon atoms,

b) a 5- or 6-membered aromatic optionally benzo-fused heterocyclic moiety having one to three atoms selected from the group consisting of S, N, and O, wherein the substituents (a) and (b) can in turn be optionally substituted with one or three $-NO_2$, CF_3, halo, -CN, OH, phenyl, C_{1-5} alkyl, C_{1-5} alkoxy, or C_{1-5} acyl,

c) morpholinyl,

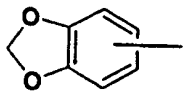
d) OH,

e) C_{1-6} alkoxy,

f) $-NR_{48}R_{49}$ in which R_{48} and R_{49} are as defined above,

g) $-C(=O)-R_{59}$, or

h)



;

R_{53} is

a) H,

b) formyl,

c) C_{1-4} alkyl,

d) C_{1-4} acyl,

e) phenyl,

f) C_{3-6} cycloalkyl,

g) $-P(O)(OR_{37})(OR_{38})$, or

h) $-SO_2R_{39}$, in which R_{37}, R_{38} and R_{39} are as defined above;

R_{59} is

a) morpholinyl,

b) OH, or

c) C_{1-6} alkoxy;

h is 1, 2, or 3;

i is 0, 1, or 2;

j is 0, or 1;

k is 3, 4, or 5;

r is 1, 2, 3, 4, 5 or 6;

t is 0, 1, 2, 3, 4, 5, or 6;

u is 1 or 2; and

Q is

a) hydrogen,

b) halo,

c) NO_2,

d) N_3,

e) C_1-C_6 alkylthio,

f) C_1-C_6 alkyl—$\overset{O}{\overset{\|}{S}}$—,

g) C_1-C_6 alkyl—$\overset{O}{\overset{\|}{\underset{O}{\underset{\|}{S}}}}$—,

h) C_1-C_6 alkyl,

i) C_1-C_6 alkoxy,

j) formyl,

k) C_1-C_6 alkyl—$\overset{O}{\overset{\|}{C}}$—,

l) C_1-C_6 alkyl—O-$\overset{O}{\overset{\|}{C}}$—,

m) -sulfamoyl (H_2NSO_2-),

n) -NHOH,

o) C_1-C_6 alkyl—$\overset{O}{\overset{\|}{C}}$-O—,

p) heteroaryl —$\overset{O}{\overset{\|}{C}}$— in which heteroaryl is a 5- or 6-membered aromatic heterocyclic group having 1-3 hetero atoms selected from O, N or S,

q) $C_6H_5-\overset{O}{\overset{\|}{C}}-$,

r) amino,

s) C_1-C_6 alkylamino,

t) di(C_1-C_6 alkyl)amino-,

u) (C_1-C_6) alkyl$-\overset{O}{\overset{\|}{C}}-NR_{60}R_{61}$ in which R_{60} and R_{61} are each independently hydrogen or C_1-C_6 alkyl,

v) OH,

w) cyano,

x) hydroxy (C_1-C_6 alkyl),

y) C_1-C_6 alkyl$-S-\overset{O}{\overset{\|}{C}}-$,

z) $NC-(CH_2)_r-\overset{O}{\overset{\|}{C}}-$ in which r is 1-6,

aa) $C_6H_5CH_2-O-\overset{O}{\overset{\|}{C}}-$,

bb) $C_6H_5-O-\overset{O}{\overset{\|}{C}}-$,

cc) C_1-C_6 alkyl$-\overset{OR_{84}}{\overset{N}{\overset{\|}{C}}}-$ in which R_{84} is hydrogen or C_{1-6} alkyl,

dd) $R_{85}O-(CH_2)_{1-6}-\overset{O}{\overset{\|}{C}}-$ in which R_{85} is hydrogen, C_{1-8} alkyl optionally substituted with one or more F, Cl, OH, C_{1-8} alkoxy or C_{1-8} acyloxy, C_{3-6} cycloalkyl or C_{1-8} alkoxy;

ee) $H-\overset{N-OR_{84}}{\overset{\|}{C}}-$ in which R_{84} is hydrogen or C_{1-6} alkyl,

ff) a substituted or unsubstituted C_6-C_{10} aryl moiety,

gg) a substituted or unsubstituted monocyclic or bicyclic, saturated or unsaturated, heterocyclic moiety having 1-3

atoms selected from O, N or S, said ring being bonded via a ring carbon or nitrogen to the phenyl substituent,

hh) a monocyclic or bicyclic substituted or unsubstituted heteroaromatic moiety having 1-3 hetero atoms selected from O, N or S, said ring being bonded via a ring carbon or nitrogen to the phenyl substituent and wherein the heteroaromatic moiety can additionally have a fused-on benzene or naphthalene ring;

the substituents for such p, q, ff, gg and hh moieties being selected from 1 or 2 of the following:

1) halo,

2) C_{1-6} alkyl,

3) NO_2,

4) N_3,

5) C_1-C_6 alkyl $-\overset{O}{\overset{\|}{S}}-$,

6) C_1-C_6 alkyl $-\overset{O}{\overset{\|}{S}}(=O)-$,

7) formyl,

8) C_1-C_6 alkyl $-\overset{O}{\overset{\|}{C}}-$,

9) C_1-C_6 alkyl $-O-\overset{O}{\overset{\|}{C}}-$,

10) heteroaryl $-\overset{O}{\overset{\|}{C}}-$ in which heteroaryl is a 5- or 6-membered aromatic heterocyclic group having 1-3 hetero atoms selected from O, N or S,

11) $C_6H_5-\overset{O}{\overset{\|}{C}}-$,

12) $-(C_1$-$C_6)$ alkyl $-\overset{O}{\overset{\|}{C}}-NR_{60}R_{61}$ in which R_{60} and R_{61} are each independently hydrogen or C_1-C_6 alkyl,

13) OH,

14) hydroxy (C_1-C_6 alkyl),

15) C_1-C_6 alkyl—S-C(=O)—,

16) NC—$(CH_2)_r$—O-C(=O)— in which r is 1-6,

17) $C_6H_5CH_2$—O-C(=O)—,

18) $-CH_2-R_{80}$ in which R_{80} is

a) $-OR_{32}$ in which R_{32} is as defined above,

b) $-SR_{32}$ in which R_{32} is as defined above,

c) $-NR_{32}R_{33}$ in which R_{32} and R_{33} are as defined above, or

d) 5- or 6-membered heteroaromatic containing 1-4 O, S or N atoms,

19) C_1-C_6 alkyl—C(=N-OR_{84})— in which R_{84} is as defined above,

20) cyano,

21) carboxyl,

22) CF_3,

23) C_1-C_6 alkyl—C(=O)-O—,

24) C_6H_5-O-C(=O)— in which the phenyl moiety may be optionally substituted by halo or (C_1-C_6)alkyl,

25) $NR_{60}R_{61}$—C(=O)— in which R_{60} and R_{61} are as defined above,

26) R_{91}-NH-C(=O)— or R_{91}-C(=O)-NH— in which R_{91} is a 5- or 6-membered aromatic heterocyclic group having 1-3 O, N or S,

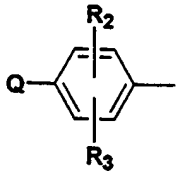
27) $C_6H_5(CH_2)_{1-6}-O-\overset{O}{\overset{\|}{C}}-$,

28) $R_{85}O-(CH_2)_{1-6}-O-\overset{O}{\overset{\|}{C}}-$ in which R_{85} is as defined above,

29) $SiR_{99}R_{100}R_{101}-O-CH_2-\overset{O}{\overset{\|}{C}}-$ in which R_{99}, R_{100} and R_{101} are each independently C_{1-6} alkyl; or

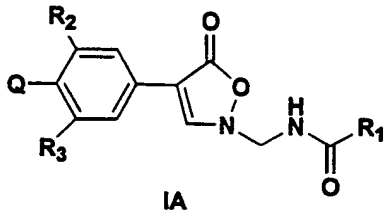
Q and either R_1 and R_2 taken together form $-O-CH_2-O$.

2. A compound of claim 1 wherein A is



in which Q, R_2 and R_3 are as defined in claim 1.

3. A compound of the formula



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or a pharmaceutically acceptable salt thereof, in which

R_1 is H, C_{1-8} alkyl optionally substituted with one or more F, Cl, OH, C_{1-8} alkoxy, or C_{1-8} acyloxy, C_{3-6} cycloalkyl or C_{1-8} alkoxy;

R_2 and R_3 are each independently

a) H,

b) F,

c) Cl,

d) Br,

e) C_{1-6} alkyl,

f) NO_2,

g) I,

h) C_{1-6} alkoxy,

i) OH

j) amino, or

k) cyano; and

Q is

a) hydrogen,

b) halo,

c) NO_2,

d) N_3,

e) C_1-C_6 alkylthio,

f) C_1-C_6 alkyl $-\overset{O}{\overset{\|}{S}}-$,

g) C_1-C_6 alkyl $-\overset{O}{\overset{\|}{\underset{O}{\underset{\|}{S}}}}-$,

h) C_1-C_6 alkyl,

i) C_1-C_6 alkoxy,

j) formyl,

k) C_1-C_6 alkyl $-\overset{O}{\overset{\|}{C}}-$,

l) C_1-C_6 alkyl $-O-\overset{O}{\overset{\|}{C}}-$,

m) C_1-C_6 alkyl $-\overset{O}{\overset{\|}{C}}-O-$,

n) heteroaryl—C(=O)— in which heteroaryl is a 5- or 6-membered aromatic heterocyclic group having 1-3 hetero atoms selected from O, N or S,

o) C_6H_5–C(=O)—,

p) amino,

q) C_1-C_6 alkylamino-,

r) di(C_1-C_6 alkyl)amino-,

s) (C_1-C_6) alkyl—C(=O)–$NR_{60}R_{61}$,in which R_{60} and R_{61} are each independently hydrogen or C_1-C_6 alkyl,

t) OH,

u) cyano,

v) hydroxy (C_1-C_6 alkyl),

w) C_1-C_6 alkyl—S–C(=O)—,

x) NC—$(CH_2)_r$—O–C(=O)— in which r is 1-6,

y) $C_6H_5CH_2$—O–C(=O)—,

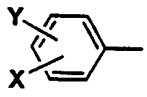
z) C_6H_5–O–C(=O)—,

aa) C_1-C_6 alkyl—C(=N–OR_{84})— wherein R_{84} is hydrogen or C_{1-6} alkyl,

bb) $R_{85}O$–$(CH_2)_{1-6}$—C(=O)— in which R_{85} is hydrogen, C_{1-8} alkyl optionally substituted with one or more F, Cl, OH, C_{1-8} alkoxy or C_{1-8} acyloxy, C_{3-6} cycloalkyl or C_{1-8} alkoxy,

cc) H–C(=N–OR_{84})— in which R_{84} is as defined above,

dd)



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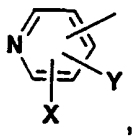

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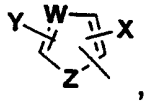

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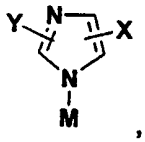

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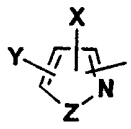

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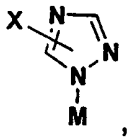

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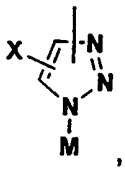

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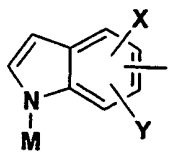

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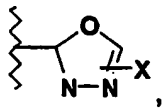

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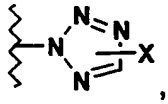

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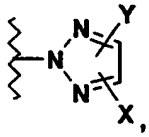

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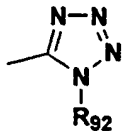
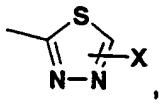


in which R_{92} is H or C_{1-6} alkyl,

pp)



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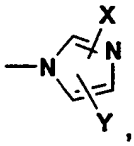

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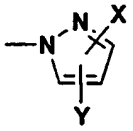

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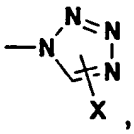
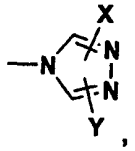
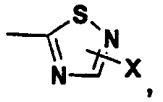


tt)



uu)



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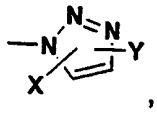

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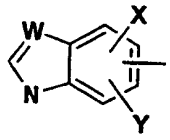

xx)

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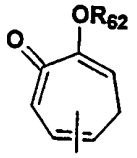

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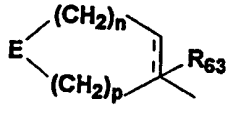


aaa) a diazinyl group optionally substituted with X and Y,

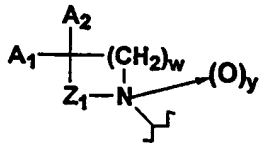
bbb) a triazinyl group optionally substituted with X and Y,

ccc) a quinolinyl group optionally substituted with X and Y,

ddd) a quinoxalinyl group optionally substituted with X and Y,

eee) a naphthyridinyl group optionally substituted with X and Y,

fff)



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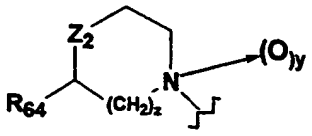
ggg)



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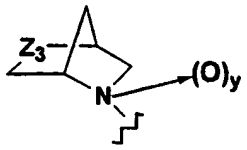
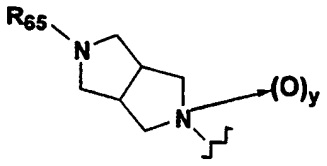


, or

iii)



;

B is an unsaturated 4-atom linker having one nitrogen and three carbons;

M is

a) H,

b) C_{1-8} alkyl,

c) C_{3-8} cycloalkyl,

d) $-(CH_2)_mOR_{66}$, or

e) $-(CH_2)_nNR_{67}R_{68}$;

Z is

a) O,

b) S or

c) NM;

W is

a) CH,

b) N or

c) S or O when Z is NM;

X and Y are each independently

a) hydrogen,

b) halo,

c) NO_2,

d) N_3,

e) C_{1-6} alkythio,

f) C_1-C_6 alkyl $-\overset{O}{\overset{\|}{S}}-$,

g) C_1-C_6 alkyl $-\overset{O}{\overset{\|}{\underset{O}{\underset{\|}{S}}}}-$,

h) C_1-C_6 alkyl,

i) C_1-C_6 alkoxy,

j) formyl,

k) C_1-C_6 alkyl $-\overset{O}{\overset{\|}{C}}-$,

l) C_1-C_6 alkyl $-O-\overset{O}{\overset{\|}{C}}-$,

m) heteroaryl $-\overset{O}{\overset{\|}{C}}-$ in which heteroaryl is a 5- or 6-membered aromatic heterocyclic group having 1-3 hetero atoms selected from O, N or S,

n) $C_6H_5-\overset{O}{\overset{\|}{C}}-$,

o) amino,

p) C_1-C_6 alkylamino-,

q) di (C_1-C_6 alkyl)amino-,

r) -(C_1-C_6) alkyl–C(=O)–$NR_{60}R_{61}$ in which R_{60} and R_{61} are each independently hydrogen or C_1-C_6 alkyl,

s) OH,

t) hydroxy (C_1-C_6 alkyl),

u) C_1-C_6 alkyl—S–C(=O)—,

v) NC–$(CH_2)_r$—O–C(=O)— in which r is 1-6,

w) $C_6H_5CH_2$—O–C(=O)—,

x) C_6H_5–O–C(=O)—,

y) C_1-C_6 alkyl—C(=N–OR_{84})— in which R_{84} is as defined above,

z) cyano,

aa) carboxyl,

bb) CF_3,

cc) mercapto,

dd) C_1-C_6 alkyl—C(=O)–O—,

ee) C_6H_5–O–C(=O)— in which the phenyl moiety may be optionally substituted by halo or C_1-C_6 alkyl,

ff) $C_6H_5(CH_2)_{1-6}$—O–C(=O)—,

gg) $R_{85}O$–$(CH_2)_{1-6}$—C(=O)— in which R_{85} is as defined above, or

hh) $SiR_{99}R_{100}R_{101}$–O–CH_2–C(=O)— in which R_{99}, R_{100} and R_{101} are each independently C_{1-6} alkyl; or

Q and either R_1 and R_3 taken together form –O-CH_2-O;

R_{62} is

a) H,

b) C_{1-8} alkyl optionally substituted with one or more halos, or

c) C_{1-8} alkyl optionally substituted with one or more OH, or C_{1-8} alkoxy;

E is

a) NR_{69},

b) $-S(=O)_i$ in which i is 0, 1 or 2, or

c) O;

R_{63} is

a) H,

b) C_{1-6} alkyl,

c) $-(CH_2)_q$-aryl, or

d) halo;

R_{66} is H or C_{1-4} alkyl;

R_{67} and R_{68} are each independently H or C_{1-4} alkyl, or $NR_{67}R_{68}$ taken together are $-(CH_2)_m-$;

R_{69} is

a) H,

b) C_{1-6} alkyl,

c) $-(CH_2)_q$-aryl,

d) $-CO_2R_{81}$,

e) COR_{82},

f) $-C(=O)-(CH_2)_q-C(=O)R_{81}$,

g) $-S(=O)_z-C_{1-6}$ alkyl,

h) $-S(=O)_z-(CH_2)_q$-aryl, or

i) $-(C=O)_j$-Het in which j is 0 or 1;

Z_1 is

a) $-CH_2-$, or

b) $-CH(R_{70})-CH_2-$;

Z_2 is

a) $-O_2S-$,

b) $-O-$,

c) $-S-$,

d) $-SO-$, or

e) $-N(R_{71})-$;

Z_3 is

a) S,

b) SO,

c) SO_2, or

d) O;

A_1 is H or CH_3;

A_2 is

a) H,

b) OH-,

c) CH_3CO_2-,

d) CH_3-,

e) CH_3O-,

f) $R_{72}O-CH_2-C(O)-NH-$,

g) $R_{73}O-C(O)-NH-$,

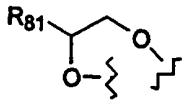
h) $R_{73}-C(O)-NH-$,

i) (C_1-C_2)alkyl-O-C(O)-, or

j) $HO-CH_2$; or

A_1 and A_2 taken together are

a)



or

b) O = ;

R_{64} is H or CH_3-;

m is 4 or 5;

n is 0, 1, 2, 3, 4 or 5;

y is 0 or 1;

p is 0, 1, 2, 3, 4 or 5;

w is 1, 2 or 3;

q is 1, 2, 3 or 4;

z is 0 or 1;

R_{65} is

a) $R_{74}OC(R_{75})(R_{76})$-C(O)-,

b) $R_{77}OC(O)$-,

c) $R_{78}(O)$-,

d) R_{79}-SO_2-, or

e) R_{80}-NH-C(O)-;

R_{70} is H or (C_1-C_3)alkyl;

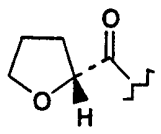
R_{71} is

a) $R_{74}OC(R_{75})(R_{76})$-C(O)-,

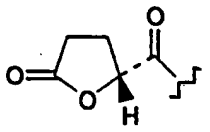
b) $R_{77}O$-C(O)-,

c) R_{78}-C(O)-,

d)



e)

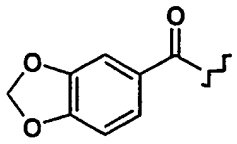


,

f) H_3C-C(O)-$(CH_2)_2$-C(O)-,

g) R_{79}-SO_2-,

h)



,

i) R_{80}-NH-C(O)-,

R_{72} is

a) H,

b) CH_3,

c) phenyl -CH_2-, or

d) $CH_3C(O)$-;

R_{73} is (C_1-C_3)alkyl or phenyl;

R_{74} is H, CH_3, phenyl-CH_2- or CH_3-C(O)-;

R_{75} and R_{76} are each independently H or CH_3, or R_{75} and R_{76} taken together are –CH_2CH_2-;

R_{77} is (C_1-C_3)alkyl or phenyl;

R_{78} is H, (C_1-C_4)alkyl, aryl-$(CH_2)_{n1}$, ClH_2C, Cl_2HC, FH_2C-, F_2HC- or (C_3-C_6)cycloalkyl;

R_{79} is CH_3; -CH_2Cl, -$CH_2CH{=}CH_2$, aryl or -CH_2CN;

R_{80} is –$(CH_2)_{n1}$-aryl where n^1 is 0 or 1;

R_{81} is

a) H,

b) C_{1-6} alkyl optionally substituted with one or more OH, halo or CN,

c) $-(CH_2)_q$–aryl in which q is as defined above, or

d) $-(CH_2)_q$–OR_{83} in which q is as defined above;

R_{82} is

a) C_{1-6} alkyl optionally substituted with one or more OH, halo or CN,

b) $-(CH_2)_q$-aryl in which q is as defined above, or

c) $-(CH_2)_q$-OR_{83} in which q is as defined above;

R_{83} is

a) H,

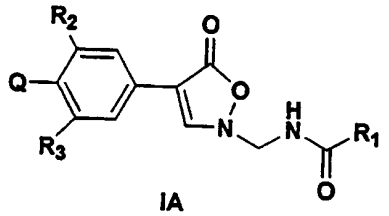
b) C_{1-6} alkyl,

c) $-(CH_2)_q$-aryl in which q is as defined above; or

d) $-C(=O)$ C_{1-6} alkyl; and

aryl is phenyl, pyridyl or naphthyl, said phenyl, pyridyl or naphthyl moieties being optionally substituted by one or more halo, -CN, OH, SH, C_{1-6} alkoxy or C_{1-6} alkylthio.

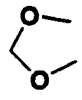
4. A compound of the formula



IA

or a pharmaceutically acceptable salt thereof, in which

R_1 is H, C_{1-8} alkyl optionally substituted with one or more F, Cl, OH, C_{1-8} alkoxy or C_{1-8} acyloxy, C_{3-6} cycloalkyl or C_{1-8} alkoxy;

R_2 and R_3 are each independently H or F; or R_2 and R_3 taken together represent  ;

Q is

a) hydrogen,

b) halo,

c) N_3,

d) NO_2,

e) C_1-C_6 alkylthio,

f) C_1-C_6 alkyl—$\overset{O}{\overset{\|}{S}}$—,

g) C_1-C_6 alkyl—$\overset{O}{\overset{\|}{\underset{O}{\underset{\|}{S}}}}$—,

h) C_1-C_6 alkyl,

i) C_1-C_6 alkoxy,

j) formyl,

k) C_1-C_6 alkyl—$\overset{O}{\overset{\|}{C}}$—,

l) C_1-C_6 alkyl—O-$\overset{O}{\overset{\|}{C}}$—,

m) C_1-C_6 alkyl—$\overset{O}{\overset{\|}{C}}$-O—,

n) $(C_1$-C_6 alkoxy$)_2$N-,

o) 5- or 6-membered heterocyclic containing 1-3 O, N or S and linked to the phenyl substituent via a carbon or nitrogen, said heterocycle moiety being optionally substituted by R_{96},

p) C_1-C_6 alkyl—$\overset{OH}{\overset{|}{\underset{\|}{N}}}$—C,

q) phenyl optionally substituted by R_{96}, or

r) 5- or 6-membered saturated or unsaturated heterocyclic containing 1-3 O, N or S and linked to the phenyl substituent via a carbon or nitrogen, said heterocycle moiety being optionally substituted by R_{96}, and

R_{96} is

a) C_1-C_6 alkyl-OH,

b) C_1-C_6 alkyl—O-C(=O)—,

c) CH_3—C(=O)— C_1-C_6 alkyl—C(=O)—,

d) cyano,

e) formyl,

f) H-C(=N-OH)— ,

g) C_1-C_6 alkyl—O-C(=O)—,

h) $SiR_{84}R_{85}R_{86}$-O-C(=O)— in which R_{84}, R_{85} and R_{86} are each independently C_1-C_6 alkyl,

i) CH_3—S(=O)(=O)— C_1-C_6 alkyl—S(=O)(=O)—,

j) $HC{\equiv}CCH_2OC(=O)$—,

k) C_6H_5-O-C(=O)— where the phenyl may be optionally substituted by halo,

l) HO-CH_2-C(=O)—,

m) $(C_1$-C_6 alkyl$)_2$N-,

n) C_1-C_6 alkyl-NH-,

o) amino.

p) C_1-C_6 alkyl—$\overset{O}{\overset{\|}{S}}$—,

q) $C_6H_5CH_2O\overset{O}{\overset{\|}{C}}$—, or

r) R_{98}–$\overset{O}{\overset{\|}{C}}$— in which R_{98} is phenyl, 5- or 6-membered heteroaryl containing 1-3 O, N or S and linked to the phenyl substituent via a ring carbon atom or 5- or 6-membered saturated or unsaturated heterocyclic containing 1-4 O, N or S and linked to the phenyl substituent via a ring carbon atom.

5. A compound selected from the group consisting of the compounds of Examples 1-97 described in the specification.

6. A pharmaceutical composition comprising a compound of Claim 1 in admixture with a pharmaceutically acceptable adjiwant, diluent or carrier.

7. A method of treating a bacterial infection in a mammal which comprises administering a therapeutically effective amount of a compound of Claim 1 to a mammal in need thereof.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/19265

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61K 31/42; C07D 261/12
US CL :Please See Extra Sheet.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 548/243, 255; 546/209; 544/58.2, 60, 137, 229, 367; 514/ 63, 227.8, 236.8, 252, 326, 359, 380

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

EAST

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAS ONLINE, WEST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,523,403 (BARBACHYN) 04 June 1996, see entire document.	1-7

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 05 NOVEMBER 1999	Date of mailing of the international search report 22 DEC 1999
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer JOSEPH K. MCKANE Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/19265

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

548/243, 255; 546/209; 544/58.2, 60, 137, 229, 367; 514/ 63, 227.8, 236.8, 252, 326, 359, 380